THE EFFECTS OF PREDICTABILITY ON STRESS AND IMMUNE FUNCTION

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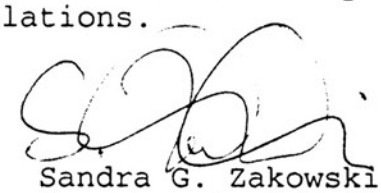

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Abstract

Title of Dissertation: The Effects of Predictability on Stress and Immune Function in Humans

Sandra G. Zakowski, Doctor of Philosophy, 1993

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Acute laboratory stressors have been shown to cause immune function changes. Mediators of stress that reduce the stressfulness of an event may attenuate the immunological effects of a stressor. Information enhancing predictability of a stressful event is one such mediator and may reduce the impact of a given stressor. The present study assessed whether predictability can reduce the impact of a stressor on psychological, cardiovascular, and immunological responses.

The effects of a predictable and an unpredictable acute stressor on self-reported distress, cardiovascular reactivity, behavioral aftereffects, and immune function in humans were examined. Thirty-six male volunteers were randomly assigned to the stressor or control conditions. Two groups completed ten trials of a cold pressor task and one group completed a comparable warm pressor control task. One of the stressor groups was given predictability over the duration of the cold pressor trials by hearing the seconds being counted down from beginning to end of each trial (predictable stressor), whereas the other stressor group received no duration predictability (unpredictable stressor).

Contrary to expectations, pain and distress reporting was significantly higher in the predictable stressor group. Cardiovascular effects were mixed with heart rate being higher in the predictable group, systolic blood pressure reactivity being higher in the unpredictable group, and diastolic blood pressure comparable in the two stressor groups. No aftereffects on frustration

tolerance on the Feather task were found. Lymphocyte proliferation to Con A (10 ug/ml) was significantly reduced only in response to the unpredictable stressor. Proliferation to PWM followed similar response patterns but was not statistically significant. Correlations suggest that high psychological and cardiovascular stress responding was associated with lower proliferation values.

The study shows that predictability is an important determinant of the impact of a stressor on various systems and that a multi-level measurement approach is necessary in order to capture the complexities of the interplay of psychological and physiological stress responding. Results are discussed in terms of the effects of information on attention to the stressor, the role of endogenous opioid peptides on immunity, and the potential adaptive value of predictability.

The Effects of Predictability on Stress and Immune Function

in Humans

by

Sandra Gabriele Zakowski

Dissertation submitted to the Faculty of the Department of Medical Psychology Graduate Program of the Uniformed Services University of the Health Sciences in partial fulfillment of the requirements for the degree of Doctor of Philosophy 1993.

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Introduction

Overview

Loss of either predictability or control can have deleterious effects on an individual's psychological as well as physical well-being. It has been shown that the same event is experienced as more stressful when it is unpredictable than when it is predictable and that providing certain kinds of information can be beneficial for a person's physical health (e.g. Schulz, 1976). Stress has been associated with an increased incidence of infectious illnesses as well as reductions in immunocompetence which is thought to be responsible for stress-related infectious illness. Finding ways to reduce stress-induced immunosuppression by alleviating the perceived stressfulness of an event or by finding mediators that can mitigate stress experience or responses is an important goal in health psychology and for prevention of disease.

The present laboratory study was designed to address the potential stress-moderating effects of predictability. The aims of this study were two-fold. First, it determined whether a given stressor is less stressful, measured in terms of perceived stressfulness, behavioral aftereffects, and cardiovascular responsiveness, when it is predictable than when it is unpredictable. Second, it assessed whether the mitigating effects of predictability would generalize to the immunosuppressive consequences of stress, i.e. does predictability buffer the reduction in immune function usually seen in response to stress? These hypotheses were tested in an acute laboratory stress model that allowed control of behavioral and psychological confounds usually encountered in naturalistic settings.

Stress

Stress has been studied from many different perspectives including physiological, behavioral, and emotional. A brief review of the history of stress research will provide a better understanding of the stress concept. Cannon (1929, 1935) first used the term 'stress' to describe an adaptive process that occurred in response to physical and emotional stimuli, permitting an organism to better fight or flee from the given stimuli. Later, Selye (1956), conducting research on the effect of a variety of aversive stimuli on laboratory animals, found a consistent triad of responses including adrenal cortical hypertrophy, thymic involution, and duodenal ulcers. These effects were thought to be non-specific because they seemed to be elicited by a wide range of stimuli. Mason (1974), on the other hand, believed that different stimuli could evoke different patterns of responses and emphasized the importance of measuring a large spectrum of neuroendocrine responses. Further, he realized that the psychological component of stress was necessary to elicit endocrine changes in his experiments. Lazarus (1966) went further in his emphasis of psychological processes in stress by identifying psychological appraisal as a necessary element in the stress process. According to Lazarus a stimulus becomes stressful only if it is appraised as threatening, harmful, or challenging. Then the availability of coping mechanisms help determine whether and how the stressor can be eliminated or whether the stress experience can be attenuated.

More recently stress has been defined as a process by which an individual responds in order to preserve his/her well-being when faced with threatening or harmful situations (Baum, Singer and Baum, 1981). Stressors can range in severity from relatively minor daily hassles to catastrophic events and can originate from immediate external environmental events or internal representations of threat such as thoughts about possible danger when no actual danger is present.

It is the appraisal of the event that determines its stressfulness and what kind of coping strategies will be used in order to reduce potential harm to the organism. These coping processes can be directed at various aspects of the stress experience.

Theoretically, coping can be viewed as a means of establishing control over one's environment or over how the environment is experienced. Even when direct action to eliminate or reduce the source of the stressor is not possible an individual may assume control by alleviating the stress experience through palliative coping (e.g. reappraising the situation as non-threatening or regulating emotional distress through relaxation or use of psychoactive drugs). Any such behavior used to cope with a stressful situation can make an individual feel that he/she has mastered the situation and is therefore in control. Several studies have shown that when given the opportunity to control an aversive event, even when no action is taken, individuals experience the situation as less stressful and show reduced stress-related responses (e.g. Carr & Wilde, 1988; Corah & Boffa, 1970; Glass & Singer, 1972; Lundberg & Frankenhaeuser, 1978). It is when this opportunity to control is lost or efforts to control a situation are unsuccessful that deleterious effects such as learned helplessness can be observed (Seligman, 1975).

Another way of attempting to gain control is by seeking information about one's environment so as to be able to predict outcomes and be prepared to cope with a given event. This is particularly important since much effort in the coping process is spent anticipating events and the more information that is available the more efficient an individual can be in preparing for the event and in choosing effective coping strategies (see Cohen & Lazarus, 1979). Anticipatory coping can help reduce the impact of a stressor and change one's appraisal of the event when it actually takes place. For example, when patients are given sensory and coping information preoperatively, they tend to have a less problematic recovery after surgery (e.g. Schmitt & Woolridge, 1973). The evidence for potential mitigating effects of information and

predictability will be reviewed in detail later.

It has already been established that responses to a stressor, once an event has been appraised as such, can include behavioral, cognitive, and emotional changes that serve to help master the stressful event. Physiological changes also serve an adaptive function in that they mobilize the organism for action and support behavioral or psychological coping (Baum, 1990). Secretion of epinephrine (E), norepinephrine (NE), corticosteroids, thyroid and growth hormones, and other neuroendocrines increase during stress and these hormones are thought to promote catabolic mobilization of energy resources (Mason, 1974). Many of these changes have been shown to be reliable indicators of the stressfulness of a given event. As Cannon (1929) noted, catecholamine release from the adrenal medulla increases when the organism is subjected to stress and serves to mobilize the body and facilitate the fight or flight response. These hormones are associated with cardiovascular changes such as increased heart rate, increases in blood pressure, and increased blood flow to skeletal muscle. Rises in adrenocorticotropic hormone (ACTH) and corticosteroids (Selye, 1955) also serve similar physiological functions mobilizing the organism to deal with the stressor.

Several factors are thought to modulate neuroendocrine responses to stress. Mason, for example, observed the occurrence of two distinct patterns. One consisted of elevated corticosteroids, NE, thyroid stimulating hormone (TSH), and thyroxine and was observed in situations of conflict or avoidance. The other pattern, increased corticosteroids, E, and NE, was seen mainly in situations of uncertainty, ambiguity, and unpredictability. Coping effectiveness is also thought to modulate the impact of stress on neuroendocrine responses (e.g. Wolff, Friedman, Hofer, & Mason, 1964). A sense of control over one's environment can have similar effects. This has been extensively demonstrated in laboratory studies of controllable and uncontrollable stressors (e.g. Breier et al., 1987).

One way of measuring stress-related physiological changes is by exposing an individual to an acute stressor in a controlled laboratory setting and measuring the hemodynamic and endocrine changes that result. Reactivity to the stressor is assessed by examining stress-related changes from resting baseline levels in blood pressure, heart rate, or some other reliable index of the stress response. Examining the effects of acute laboratory stressors has been useful in trying to determine psychological and physiological mechanisms underlying the stress response. The effects of different types of stressors, availability of mediating factors such as perceived control, and the availability of different coping mechanisms are being explored in order to examine the impact of stress. Also, the interaction of different hormonal and physiological response patterns to different types of stressors has been examined.

Stress and health

The concept of stress and coping becomes more important when its value in predicting health and illness is considered. The impact of stress on the general well-being of the organism was already described by Selye's general adaptation syndrome (GAS) which included three stages of response to a stressor (Selye, 1956). First, when confronted with a threat the body mobilizes its coping resources in what he called the alarm reaction. This is followed by a stage of resistance which constitutes a state of adequate adaptation. If demands or threats associated with the stressor persist or are repeated the organism may not be able to adapt and reaches a stage of exhaustion in which the body's defenses are depleted and disease is more likely to occur.

Different types of stressors ranging in severity have been studied in this context. Stressful life events, for example, measured by inventories such as Holmes and Rahe's (1967) Social Readjustment Rating Scale, have been associated with increased incidence of diagnosed infectious illness, heart disease, and symptom reporting. Immune-related diseases such as upper

respiratory infections and mononucleosis have also been related to stressful events. For example, Meyer and Haggerty (1962) found a relationship between family-related stressors and respiratory infections in children. Greater frequency of upper respiratory illnesses was also noted among adult male prisoners who reported high distress when compared to low stress inmates (McClelland, Alexander, & Marks, 1982). More recently, subjects who were administered different cold viruses were more likely to contract respiratory infection and clinical symptoms if they reported experiencing high stress than if they had low self-reports of stress (Cohen, Tyrell, & Smith, 1991). A study of mononucleosis incidence in West Point cadets found that high career motivation and poor performance (a presumably stressful situation) were associated with increased risk for mononucleosis (Kasl, Evans, & Niederman, 1979). While research on stressful events and illness is abundant (for reviews see Cohen & Williamson, 1991; Jemmott & Locke, 1984) there are obvious problems with the predominantly retrospective nature of these studies. In many of the studies, for example, it is unclear whether the illness itself may have been a cause of the high stress reporting.

Several mechanisms have been proposed to explain a stress-illness link. One way that stress may affect health is through behavioral changes that occur as part of the coping process. When confronted with a stressor an individual has several coping options available, including emotion-focused and palliative coping strategies which are geared towards reappraising the situation in a way that makes it less threatening or towards reducing one's emotional distress (Lazarus & Folkman, 1984). Palliative coping often involves the use of drugs such as alcohol, nicotine, or illicit drugs that alter one's perception of the stressor and make its experience less aversive.

Alternatively, problem-focused coping consists of direct action on the source of the stress itself. The work associated with this kind of coping may also lead a person to engage in a life

style in which neglect of health practices such as exercise and a healthy diet becomes common. In addition, the physiological changes that occur during stress have direct physiological effects that are associated with stress-related illness. Although, many of these changes serve immediate adaptive functions when the organism is faced with a stressor, these bodily changes may in the long run produce wear and tear and have pathogenic effects as has been evidenced by the development of atherosclerosis, hypertension, and heart disease (Schneiderman, 1983; Krantz & Manuck, 1984).

Some 'stress hormones', such as catecholamines and cortisol, have recently been associated with immunological changes (e.g., Ben-Eliyahu, Yirmiya, Liebeskind, Taylor, & Gale, 1991; Riley, 1981). This observation is directly relevant to the stress-health relationship since an altered immune system may not be efficient in protecting the body from the pathogens that can cause illness and may facilitate development of infectious illnesses or reduce the body's ability to reject tumors.

Stress and immune function

Stress has been associated with various types of illnesses that suggest immune system involvement. A number of studies have examined the relationship between stressful life events and infectious disease (Cohen, Tyrell, & Smith, 1991; Cohen & Williamson, 1991; Jemmott & Locke, 1984). In order to determine the pathways of this rather well established stress-illness link research has examined the effects of stress on the immune system.

Several naturalistic stressors, including marital discord and divorce, job loss, death of a spouse, and medical school examinations are known to be associated with changes in immune system functioning (O'Leary, 1990). For example, men and women who are separated or divorced from their spouses show impairment of the function of several important immune

parameters, e.g. decreases in lymphocyte proliferation to mitogens and disrupted immune system control over latent viruses shown by increases in antibody titers to the virus (e.g. Kiecolt-Glaser, Fisher, Ogrocki, Stout, Speicher, & Glaser, 1987; Kiecolt-Glaser, Kennedy, Malkoff, Fisher, Speicher, & Fisher, 1988). Likewise, losing one's job and long-term unemployment (9-12 months) may be associated with decreases in in vitro lymphocyte function (Arnetz et al., 1987). Chronic stress was also experienced by residents of the Three Mile Island area who, more than six years after the accident at the nuclear power plant, exhibited greater antibody titers to latent viruses than controls (McKinnon, Weisse, Reynolds, Bowles, & Baum, 1989). The death of a spouse is another major life event that has been studied in conjunction with immunological changes, showing significant decreases in immune function in the bereaved (Bartrop, Luckhurst, Lazarus, Kiloh, & Penny, 1977; Schleifer, Keller, Camerino, Thornton, & Stein, 1983). The effects of bereavement on host defense has also been linked to depression (Irwin, Daniels, Bloom, & Weiner, 1986; Linn, Linn, & Jensen, 1984). A relatively short-lived and less dramatic stressor, i.e. medical school examinations, has also shown reliable and significant associations with decreased lymphocyte proliferation, decreased natural killer (NK) cell activity, increased antibody titers to latent viruses, decreased interleukin-2 (IL-2) receptor gene expression, etc. (e.g. Glaser et al., 1987, 1990; Kiecolt-Glaser, Garner, Speicher, Penn, & Glaser, 1984). Recently, stress and anxiety in medical students was associated with delayed seroconversion to Hepatitis B vaccination (Glaser et al., 1992). This suggests that several parts of the immune system may be suppressed even in response to a moderate and transient stressor.

Although the links between these stress-induced immune changes and clinical signs of infectious illness have not been directly studied, many of these immune parameters are known to be of importance in the progression of cancer and AIDS (Ironson, et al., 1990; Levy, Herberman, Maluish, Schlien, & Lippman, 1985). Further, reactivation of latent viruses may

lead to infectious illness (Kasl, Evans, & Niederman, 1979) and a delay in seroconversion to vaccinations may have implications for resistance to disease (Glaser et al., 1992). Stress has also been suggested to impair DNA repair in lymphocytes which may have implications for the cells' susceptibility to carcinogen-induced damage (Kiecolt-Glaser, Stephens, Lipetz, Speicher, & Glaser, 1985; Setlow, 1978).

The mechanisms by which stress effects immune system changes have primarily been studied in animals. Hormones such as cortisol, epinephrine, and norepinephrine as well as many other neuroendocrines that are released in response to stressors have been shown to directly or indirectly affect the immune system (for a review, see Dunn, 1989). Many immune organs, among them the bone marrow, spleen, thymus, and lymph nodes, are known to be innervated by sympathetic nerve fibers (see Felten & Felten, 1991), suggesting that the immune system may be affected by the same pathway as organs of other systems, such as the cardiovascular system, that are implicated in the stress-induced fight-or-flight response. Further, T- and B- lymphocytes and macrophages express beta-adrenergic receptors (Bourne et al., 1974) which may be responsive to the increased levels of catecholamines found during stress. In animals, stress-related increases in cortisol levels have been associated with more rapid tumor growth (Riley, 1981), and stress-induced elevations in catecholamines may account for the suppressive effect on NK cell activity and promotion of tumor growth (Ben-Eliyahu et al., 1991). Some human studies have examined the effects of epinephrine injection on immune system changes (e.g. Yu & Clements, 1976; Crary et al., 1983), but the results of these studies have been contradictory and difficult to interpret.

One way of studying the underlying physiological mechanisms and the contribution of different psychological states to the stress-immune system relationship is through the use of an acute laboratory stress model that has been established in cardiovascular research. By exposing

an individual to acute stressors in a controlled laboratory setting we can examine causal relationships between stress and cardiovascular, endocrine and immune responses, and by manipulating different aspects of the environment the effects of different psychological and behavioral variables can be assessed. To date, six separate studies have shown that brief exposure to a relatively mild stressor such as mental arithmetic, noise and shock, or watching a combat surgery film can induce rapid and transient changes in NK cell activity or lymphocyte proliferation within minutes of exposure to the stressor (Bachen et al., 1992; Manuck, Cohen, Rabin, Muldoon, & Bachen, 1991; Naliboff et al., 1991; Sieber et al., 1992; Weisse et al., 1990; Zakowski, McAllister, Deal, & Baum, 1992) (see Table 1 for methodological details on these studies). Manuck et al. (1991) exposed 20 male subjects to a 20-minute stressor that consisted of a computerized version of the Stroop color-word test and a mental arithmetic task. Subjects who had high cardiovascular and catecholamine reactivity to the stressors showed a significant decrease in lymphocyte responsiveness to PHA immediately after the stressor, whereas low reactors were similar to a no stress control group. In a similar study (Zakowski et al., 1992) the stressor consisted of a combat surgery film and a subsequent recall task asking subjects to speak about details of the film. The 20 males exposed to the stressor had significant decreases in lymphocyte proliferation to Con A ten minutes into the stressor when compared to nine non-stressed controls. Further, high blood pressure reactors to the film showed the largest decreases in proliferation compared to low reactors and controls. Bachen et al. (1992) administered a 21-minute computerized version of the Stroop color-word test to 33 male subjects who were compared to 11 controls. Lymphocyte proliferation to PHA was found to be relatively lower in the experimental group immediately after the task, whereas control subjects showed an increase in mitogenesis. In addition the task induced a decrease in CD4/CD8 ratios and an increase in NK cell numbers.

Naliboff et al. (1991) tested the effects of a mental arithmetic task on NK cell activity in women of two different age groups. The younger women (age 21 to 41) showed an increase in NK cell activity in response to the stressor compared to controls whereas the older group (age 65 to 85) showed no change. These results suggest that there may be gender differences in the effects of acute stressors on immune function, which may occur through differential effects of sex steroids on immune cells. For example, lymphocytes have receptors for estrogens and androgens and their ability to proliferate in vitro can be affected by these hormones (Cohen, Daniel, Gordiev, Saez, & Revilland, 1983; Wang et al., 1988). However, the possibility that stress-related immune changes are affected by these hormones still needs to be explored.

The mediating effects of perceived control have been explored in two separate studies. Weisse et al. (1990) exposed their subjects to 30 minutes of controllable or uncontrollable noise and shock. Although, exposure to the uncontrollable stressor was more effective in changing mood it did not effect changes in lymphocyte proliferation when compared to the no stress control session. The controllable stressor, however, resulted in a decrease in proliferation to Con A. Sieber et al. (1992) exposed male subjects to two 20-minute sessions of either escapable noise, inescapable noise where subjects were given perceived control, inescapable noise without perceived control, or a no noise condition. Only subjects in the inescapable noise condition who were given no instructions to control the noise showed decreases in NK cell activity; all other groups showed no significant changes. These contradictory results may be due to varying procedures and methodological problems in both studies. Some of the major differences between the two studies such as the stressor used, the duration of the manipulation, timing of blood sampling, and choice of immune measures could account for the inconsistent results. Further, both studies could have benefited from using more extensive stress assessments. The studies relied on very minimal self-report measures of stress and perceived control. A multi-

measurement approach including self-report, cardiovascular, and biochemical measures would have been more effective in determining the impact of the manipulations. Further, the fact that in both studies control was manipulated by having subjects press a button added a confound of differential activity in the groups.

Despite some variations in methodology such as differences in timing of immune measurements, stressor manipulations, and dietary restrictions prior to the experiment all of these studies showed that immune function changes can occur within a short period of time in response to acute stressors (see Table 1). The direction of the immune effects seems to vary depending on the population and the immune measures studied. However, four out of the six described studies reported a reduction in immune function as a result of stressor exposure which is consistent with the majority of field and animal studies in psychoneuroimmunology. This suggests that this laboratory method of studying the effects of stress on immunity may prove a reliable and cost effective way of studying human psychoneuroimmunology. Also by bringing this type of research into the laboratory one will be better able to control for behavioral changes associated with stress and immunity and to draw causal inferences. Some of these studies also demonstrated that this laboratory model may be sensitive enough to pick up immune changes due to stress-related psychological and physiological mediators such as perceived control and levels of cardiovascular reactivity. This method may then prove useful for the study of mechanism underlying the stress-immune system link by manipulating physiological, psychological and behavioral mediators of stress.

Stress-mediating variables

It has already been mentioned that a variety of factors can determine whether a given event is perceived as stressful and how extensive its impact may be. Perceived control is one

example of a stress mediator. It can be defined as the perceived ability to determine outcomes of an event (Gatchel, Baum, & Krantz, 1989) and has been found to significantly affect stressor appraisal and responsiveness. Information received from environmental or internal cues may aid in enhancing that sense of control by helping the individual to predict, prepare for, and explain a given event. Although perceived control and predictability are closely related concepts, predictability is also separate and distinct from perceived control because it simply addresses the amount of knowledge about an event that is received by the individual regardless of whether it can be controlled or not. Predictability can be defined as the amount of knowledge an individual perceives to have over an aspect of an event. That aspect of the event is usually something that occurs in the immediate or remote future. While information and predictability are often used interchangeably in the literature, they are somewhat distinct. Information consititutes the stimuli to which the individual is exposed but it is the stimuli that are processed and used by the individual that enhance the person's sense of predictability. It can therefore be said that information about a future event constitutes the objective stimuli that are presented to the individual and predictability is the subjective or perceived knowledge the individual has about the future. For practical purposes information and predictability are used interchangeably in this paper since information is what is used to manipulate predictability in the empirical studies and the two are rarely separated. The following section will address theories explaining how predictability can affect stress and will review the literature on laboratory studies conducted to address mechanisms associated with the stress-modulating effects of predictability.

Predictability

Many researchers and theorists have suggested that information about a potentially stressful event provides individuals with a sense of control over their environment and reduces the aversiveness of the event (e.g. Berlyne, 1960). Establishing rules for how one should feel or behave in certain situations or attempting to predict what the future will hold so as to be 'prepared', play a major role in people's lives. Although no instrumental control or direct action upon the event may be possible, certain types of information may make the event more predictable and therefore mitigate some of its stressful impact on the individual. In this section, predictability will be defined and then theories and research evidence considered.

There are at least two major types of predictability as defined in the literature. Contingency predictability provides information about when and under what circumstances a given event will occur. Seligman and his colleagues (1971) defined this type of predictability in Pavlovian conditioning terms where a relationship between a neutral stimulus and an aversive event (UCS) is arranged in such a way that the neutral stimulus predicts the occurrence or the absence of the UCS. The information can be presented in different ways: in the laboratory a signal such as a tone or light is often used, while in naturalistic settings more complex environmental cues or sets of cues or communications from other individuals may help to predict when an event will take place. Information about qualitative aspects about an event, such as intensity, duration, or information about what kind of impact a stressor will have on physical and emotional responses can also prove valuable in modifying one's expectancies and the stressfulness of the event. This second type of predictability has often been termed 'what-kind-of-event' predictability (see Miller, 1981).

When an event is made predictable, cognitive, behavioral, or physiological changes may moderate the perceived stressfulness of the event. Several theories have attempted to explain

what occurs when an event is predictable or when it is unpredictable and what is responsible for these different effects. It should be kept in mind that most research on predictability has examined the impact of negative events. Whether the same predictions hold true for positive events is an empirical question that will not be addressed here.

Two of the most often cited theories used to explain the effects of predictability are the preparatory response (PR) hypothesis and the safety-signal hypothesis. The former hypothesis postulates that when an event is predictable the individual will respond in such a way that the event will be perceived as less aversive or more appetitive (Perkins, 1968). For example, if an inevitable shock is about to occur the individual can make postural changes, etc. in order to buffer the painful effect of the stimulus even though no direct action on the source of the stimulus is possible. This implies that predictable events are preferred to unpredictable ones (e.g. Pervin 1963), that immediate events are more preferable than delayed ones because better timing of the PR is possible (e.g. D'Amato & Gumenick, 1960), and that predictable events are less aversive than unpredictable ones (e.g. Katz, 1984). However, Furedy and his colleagues have conducted a series of studies showing no preference for predictable noise or shock and no difference in aversiveness ratings of the predictable vs. the unpredictable event (see Furedy, 1975 for a review).

An alternative view was proposed by Seligman in 1968. According to his safety-signal hypothesis the presence of a cue predicting an aversive event automatically implies that the absence of that cue signals a 'safety period' during which the aversive event will not occur. The time between the last aversive stimulus and the next cue is a time during which the individual can relax. Therefore, in a predictable situation the organism will be able to spend more time resting and less time anticipating the stressor than in an unpredictable situation where the organism is more likely to be in constant fear. This theory has been tested in animals using disruption of bar-

pressing for food as an index of fear. When shock is not reliably preceded by a signal, rats will stop bar-pressing entirely and develop stomach ulcers, whereas when a signal is present rats will only stop bar-pressing from the time the signal comes on to the end of the shock stimulus and resume bar-pressing during the 'safety-period' (see Seligman et al., 1971 for a review).

A third hypothesis, the preparatory set hypothesis (Grings, 1960), refers primarily to an event's impact on physiological changes. It suggests that a predictable event generates heightened anticipatory arousal so that once the actual event occurs its impact is relatively small. Grings and his colleagues showed that in a high certainty condition anticipatory GSR was higher than in low certainty conditions but the inverse was true for the response to the event itself (Grings & Sukoneck, 1971). Similar results were found by Lykken, Macindoe, and Tellegen in 1972. This theory only explains why the impact of the predictable event itself could be less stressful but does not suggest that individuals are generally less aroused when faced with a predictable stressor situation. However, some studies do not support this hypothesis. A study on anticipatory stress by Street, Baum, and Singer (1984) found that subjects who expected a cold pressor task had higher anticipatory blood pressure responses than subjects who did not expect the task, but the two groups showed similar levels of responsiveness upon impact of the stressor.

Lazarus (1966) takes a more cognitive approach to the problem and uses the term 'event uncertainty' to distinguish his theory from the animal models. According to this view the likelihood that an event will occur modifies how this event will be appraised. If information about a future event is absent or scarce, anticipatory coping is impaired because it is impossible to know ahead of time which coping resources will be effective in mastering the event. Uncertainty about whether an event will occur can cause a great deal of conflict and confusion due to constant appraisal and reappraisal of the situation (Lazarus & Folkman, 1984). Monat, Averill, and Lazarus (1972) showed that when the timing of shock was known subjects had

different coping patterns than when the timing was unknown.

It should be noted that none of these hypotheses have received extensive empirical support and that the theories are not mutually exclusive. Rather, a combination of the different responses are likely to occur at one time. The likelihood of one response prevailing over another is probably partially determined by the circumstances and the event in question. Laboratory research on predictability can only examine part of the phenomenon occurring in real life stress situations. Lazarus and Folkman (1984) suggest that uncertainty in real life is complex and entails an intricate set of events depending on the individual and the environmental circumstances. This may account for some of the contradictory findings in the literature. According to these authors the greater the situational ambiguity or uncertainty created by the environment, the more important individual differences become in determining the responses to the situation. In that vein, Miller (1979) proposed the blunting hypothesis suggesting that there are individual and situational differences in whether a predictable or an unpredictable event is preferred. Monitoring one's environment for information about a future event may be adaptive in some situations, e.g. when the event is potentially controllable, whereas blunting, i.e. ignoring or avoiding information associated with potential threat may be preferable in other situations. Another hypothesis was proposed by Matthews and her colleagues (1980) suggesting that the mediating effects of predictability depend on how much attention is allocated to the aversive stimulus. The authors suggest that the reason why unpredictable events are more stressful is because more attention is paid to them. In fact, when subjects are forced to pay attention to both predictable and unpredictable stressors, predictability is just as stressful as unpredictability as measured by symptom reporting (Matthews, Scheier, Brunson, & Carducci, 1980).

Several studies have examined the effects of information and uncertainty on stress and health in naturalistic settings such as hospitals or nursing homes. Only a few of these were able

to separate predictability from controllability. Research on information given to patients awaiting aversive medical procedures or surgery has identified beneficial effects of predictability and cognitive control. Johnson (1973) studied subjects' responses to having their blood pressure measured with a cuff that caused ischemic pain. One group of subjects received accurate sensory information about the sensations they might feel and the other group received routine procedural information. After the procedure was completed, the first group reported significantly less emotional distress, suggesting that being able to predict the kinds of sensations subjects experienced reduced the stressfulness of the aversive procedure. Another study examined the effects of sensory vs. behavioral information on distress in patients undergoing an aversive endoscopic examination (Johnson & Leventhal, 1974). Sensory information alone was associated with less need for tranquilizers, more stable heart rates, and less gagging when compared with results in the no-information control group. Behavioral instruction was only beneficial in combination with sensory information. In other words, information that conferred the opportunity to exert control over the situation was only useful if patients could predict sensations accurately. A well-controlled study was conducted on the effects of predictability and controllability on the physical and psychological wellbeing in elderly people living in a retirement home (Schulz, 1976). Three groups of subjects were periodically visited by college students. One group could control the date, duration and frequency of the visits, one group had no control but had information about these details, and the third group received random visits without control or predictability. The controllable and predictable visits were more effective, and both the control and the predictability groups were significantly healthier, more active, and rated themselves as happier and more hopeful than the comparison group.

These field studies emphasize the importance of information about aspects of both stressful and pleasant future events on physical health and psychological well-being. However,

in a naturalistic setting, it is very difficult to control for extraneous variables and to establish mechanisms by which predictability works. For this purpose a controlled laboratory setting seems more appropriate.

Four basic experimental designs have typically been used in manipulating the different conditions in studies of predictable and unpredictable stressors in the laboratory. First, stimuli such as lights or tones have been used to signal the occurrence of the aversive event, usually a loud noise or electric shock. The interstimulus interval (ISI), i.e. the time between the signal and the aversive event, can be varied with shorter ISI's usually representing more effective predictability. A longer delay between the signal and the stressor is often used to manipulate unpredictability, the idea being that if the stressor immediately follows the signal the subject is better able to predict its timing than when there is a long delay and the subject has to try to estimate the amount of time elapsed. An alternative way of varying predictability is by presenting the aversive stimulus in variable vs. fixed intervals, so that when a stimulus is presented at constant intervals the subject's 'internal clock' will serve as a signal and make the aversive stimulus more predictable than when it is presented at variable intervals without any discernable pattern. In this design the length of the intervals can be varied with longer intervals usually being more stressful (e.g. Glass & Singer, 1972). Other studies provide subjects with a clock counting down to the next aversive stimulus, thereby diminishing reliance on the individual's judgment of time elapsed between two stimuli.

The first three methods are designed to vary predictability of <u>when</u> the stressor occurs. In order to manipulate certainty of <u>whether</u> a given stimulus will occur experimenters often vary the instructions they give to their subjects by changing the probability of the event's occurrence. In this case 100% or 0% probability levels produce the highest predictability, whereas a 50% probability level is thought to be the most unpredictable situation. In this case, however, a

potential mismatch between the objective and the individual's subjective probability has to be taken into account (Epstein & Roupenian, 1970).

Several different measures have been used to test the hypothesis that predictability mediates the stressfulness of an aversive event. Preference can be measured using self-report or a behavioral measure observing a subject's choice between the predictable and the unpredictable stimulus. Aversiveness ratings and self-reports of stress have also been widely used to determine the stressfulness of a given event. Psychophysiological measures of arousal such as heart rate (HR), skin conductance (SC), and occasionally blood pressure (BP) changes in response to the stimuli are the most commonly used measures. In some studies, changes occurring at different time points are distinguished, and the response is broken down into orienting response (OR, the response immediately following the signal), anticipatory response (AR, the response immediately preceding the aversive event), and unconditioned response (UCR, the response to the aversive event itself). In animals, physiological effects such as gastrointestinal ulceration, weight loss, and endocrine responsiveness are measured. Finally, aftereffects of stress in the form of performance or frustration tolerance on a task following the stressor period have proven useful in distinguishing stressfulness of predictable and unpredictable events. Task performance during the stressor period has also been used as a measure but has not been found to be very sensitive.

The literature concerning predictability as a mediator of stress will be reviewed by examining each of these outcome measures separately. A complete review of the animal literature on predictability is unnecessary because it would add very little to the discussion. Findings from animal studies will therefore be only briefly summarized at the beginning of each section.

Preference for predictable versus unpredictable events

For the most part the literature shows that the majority of subjects prefer predictability to unpredictability. Preference can be measured by either self-report or behavioral observation. For the first, subjects are typically exposed to both predictable and unpredictable stimuli in a within subjects design and are then asked which of the two conditions they prefer. The second kind of measure is obtained by exposing subjects to a choice procedure in which they are given the opportunity to choose between immediate vs. delayed shock or noise, between a warning signal that predicts the onset of the stimulus and some type of distraction such as music, or between a warning signal and either a signal that does not consistently predict the event or no signal at all. The latter has been used in animals usually in form of a shuttle box.

The majority of animal studies show that when given a choice between signaled and unsignaled shock, animals will choose the signaled alternative when the amount of shock given is equal in both conditions. Especially striking, however, is the finding that even when the unsignaled alternative consists of shorter and less intense shock than the signaled alternative, animals still prefer the signaled shock even though it is of longer duration and greater intensity (Badia, Culbertson, & Harsh, 1973). Although the findings seem relatively robust, some ambiguity occurs when intershock intervals or shock intensities are varied, for example, it has been suggested that animals prefer the unsignaled condition when shock intensity is very low (see Badia, Harsh, & Abbott, 1979 for a review).

As is to be expected humans are less consistent in their preferences when faced with a choice of predictable or unpredictable events. In human studies many factors, including past experience and personality variables, which are likely to influence a person's preference, need to be taken into account. Despite this complexity, most studies show that predictability is preferred by the majority of subjects and this generalizes to a variety of experimental paradigms.

When subjects were exposed to alternating immediate vs. variable delayed shock after having pressed a switch in a forced choice paradigm, 19 out of 20 subjects said they would prefer receiving immediate shock in the future (Badia, McBane, Suter, & Lewis, 1966; Experiment 2). If shock is given immediately it is perceived as more predictable. This effect does not hold up when a warning signal is added to the delayed shock condition which predicts immediate shock administration. In this case only 50% of subjects preferred the immediate shock switch since in both conditions subjects were now provided with a signal that immediately preceded shock (Badia et al., 1966; Experiment 3). Pervin (1963) obtained similar results when he exposed his subjects to either self-administered or experimenter-administered shock preceded by either a warning signal, no signal, or inconsistent signals not predicting shock. Subjects reported preferring the warning signal most and the absent signal condition least regardless of who administered the shock.

In a more recent study by Katz (1984) 64% of subjects preferred signaled shock to unsignaled shock. Maltzman and Wolff (1970) found that predictability of 110 dB white noise was preferable as well. Out of 40 subjects 36 stated they preferred receiving a signal that immediately preceded that noise to a signal that was followed by delayed noise. In a differential conditioning paradigm Furedy et al. exposed subjects to several CS+ (signal)-UCS (80-120 dBA white noise) trials and CS- (absence of UCS) and UCS alone trials. In a subsequent questionnaire 28 out of 56 subjects indicated preference for signaled noise, 12 preferred unsignaled noise (UCS alone), and 16 indicated no preference (Furedy, Fainstat, Kulin, Lasko, & Nichols, 1972).

Subjects' actual behavior in the laboratory confirms self-reports of preference. D'Amato and Gumenik (1960) gave subjects a choice between using a lever that produced immediate shock and one producing variably delayed shock and found that subjects tended to use the immediate shock lever more often. Similarly, Badia and colleagues (1966; Experiment 1) reported that over

time the majority of subjects more frequently used the lever that delivered immediate shock than the one that delivered delayed shock. Similar studies have been done offering subjects an alternative coping mechanism, i.e. distraction. Averill and Rosenn (1972) gave subjects either avoidable or unavoidable high, medium or low intensity shock and gave them the choice of listening to music or listening for a warning signal predicting the onset of shock. Vigilance was defined as spending more than 50% of the time listening for the signal. The amount of time spent listening for the signal significantly increased with the intensity of the shock and with the possibility of avoiding the shock. Generally, more subjects engaged in vigilant coping than in distraction in the avoidance condition, whereas the opposite was true for the non-avoidance condition. However, no statistics were presented for this latter finding. Another study was aimed at determining the role of avoidance in preference for predictability by varying the perceived probability at which shock could be avoided (Averill, O'Brien, & DeWitt, 1976). Subjects were more likely to choose listening to music when there was no chance of avoiding the shock and were most vigilant (chose to listen for the signal) when there was a 66% or 100% chance of avoidance. While these results suggest that information is only preferable when a possibility of control exists, a similar study done by Miller (1979) using the same choice paradigm found that subjects overall preferred the vigilant strategy regardless of whether the shock was avoidable or not but that they became less consistent vacillating back and forth between vigilance and distraction.

These studies all examined preference for contingency predictability. Lanzetta and Driscoll (1966) presented subjects with a choice of information about what kind of event (shock, no shock, award or no award) they would receive by holding contingency predictability constant. Most subjects chose to receive information regardless of whether the event was going to be positive or negative.

Although, there seems to be a general trend for preference for predictable rather than unpredictable events, in all of the studies that have been reviewed a substantial number of subjects can be found that show no preference for either predictability or unpredictability or even prefer the unpredictable option. In addition some studies failed to find preference effects, for example Furedy and his colleagues, in a series of studies reported that subjects expressed no preference for signaled vs. unsignaled shock (Furedy, Katic, Klajner, & Poulos, 1973). There may be several reasons for these inconsistencies, including personality differences. Miller (1979) found that those subjects who chose predictable shock also indicated a greater preference for information on a questionnaire giving a hypothetical situation of fear of flying. She concluded that some people may cope by monitoring their environment for information whereas others prefer to cope by denial or blunting. Further, boredom may account for some of the inconsistent responding found in the choice procedures, i.e. according to Berlyne (1960) repetitive correspondence between two events, one predicting the other, may lead to boredom and therefore increase unpleasantness. Finally, characteristics of the event may be responsible, i.e. the possibility of controlling or avoiding the event may increase the desire for predictability. In sum, the majority of people prefer predictability to unpredictability, although there does seem to be room for individual differences.

Aversiveness ratings and self-reported distress

Asking subjects how aversive they found an event to be or how stressed, angry, or frustrated they felt when the event occurred is another way of determining the impact of unpredictability and to examine whether the same event is preferable or less stressful when it is predictable vs. when it is unpredictable.

Katz (1984) administered signaled and unsignaled shock to 80 women in a within subjects

design, counterbalancing the order of presentation. Predictable shock was rated as significantly less aversive and evoked significantly less self-reported anticipatory distress than unpredictable shock. Similar results were obtained in 30 male subjects who rated signaled shock as significantly less painful and less anxiety provoking than unsignaled shock regardless of whether the experimenter or they themselves administered the shocks (Pervin, 1963). Delayed shock or noise are also perceived as more aversive. In one study (D'Amato & Gumenik, 1960) 16 out of 20 subjects rated delayed shock as more unpleasant than immediate shock and in a study of immediate vs. delayed 110 dBA noise, the delayed noise was perceived to be significantly more unpleasant (Maltzman & Wolff, 1960).

In the forced choice experiment by Badia et al. (1966; Experiment 2) 15 out of 20 subjects reported that variable delayed shock made them more anxious and tense than immediate shock, and 7 of those claimed that the variable shock was more intense. No statistics are reported for these findings. Lovibond (1968) found that irregularly occurring shock was rated to be more aversive than the same intensity shock presented at regular (predictable) intervals. Klemp and Rodin (1976) randomly varied the ISI between signal and shock to be five or 20 seconds long and manipulated the level of uncertainty by giving the high certainty group a clock counting down to predict the onset of the shock. The high certainty group reported significantly lower levels of distress than the low certainty group but no effect on perceived shock intensity was found. In addition, subjects who were told beforehand to pay attention to the stimulus rated shocks as stronger and reported greater distress than subjects who were told to attend to their emotional reactions to the shock.

Finally, Monat et al. (1972) varied temporal and event uncertainty in a group of 20 male subjects and measured tension and attention ratings during the three-minute anticipatory period.

Subjects who were uncertain about the time of occurrence of shock reported an initial increase and then a steady decrease in tension before shock administration, whereas those who knew when the shock would come had low initial but steadily increasing tension. This was paralleled by the amount of attention each group reported paying to the shock, i.e. high attention was correlated with high tension ratings. The authors concluded that people cope in different ways depending on how much they know about the timing of an event.

Reporting of physical symptoms such as headaches, racing heart, upset stomach, dizziness, and other symptoms that may be seen during stress have been shown to increase under conditions of unpredictable 95 dBA noise (Weidner and Matthews, 1978). Subjects exposed to irregular bursts of intermittent noise reported significantly more symptoms than those exposed to regular intermittent noise. A subsequent study by Matthews and her colleagues suggested that subjects in the unpredictable noise may pay more attention to the noise (Matthews et al., 1980). When subjects were instructed to pay attention to the noise both the predictable and unpredictable noise groups reported the same number of symptoms, but when no such instructions were given it was the unpredictable group that reported the most symptoms.

Several studies failed to find differences in aversiveness ratings between predictable and unpredictable events. Glass and Singer (1972) conducted a series of studies examining the effects of predictable and unpredictable noise and found no differences on subjective ratings of noise between the groups. These studies will be described in more detail later. Lykken and colleagues (1972) manipulated the predictability of when shock would occur as well as where (on what limb) it would occur. Their subjects reported the shocks to be of similar intensity regardless of whether they were predictable or not. Finally, Furedy and his colleagues designed a series of studies using differential conditioning paradigms with shock and noise and failed to find any effects of predictability on aversiveness ratings of the stimuli (e.g. Furedy & Chan, 1971; Furedy & Doob,

1972; Furedy & Ginsberg, 1973). Miller (1979), in contrast, found that subjects who chose signaled shock reported greater fear, tension, and expectation of pain than those who chose distraction.

For the most part, then, the literature indicates that predictable aversive events are perceived as less aversive and evoke fewer stress-related feelings and symptoms than unpredictable events. As for the preference data some individual variability is found. One explanation that was offered by Matthews and her colleagues (1980) and Klemp et al. (1976) is that the subjective reaction to unpredictable events may depend on the amount of attention that is paid to the aversive event, i.e. the more attention is allocated to the aversive stimulus the more stressful it may appear to be.

Task performance

When people experience stress they are thought to perform less well on simple as well as more complex mental tasks. However, with a few exceptions, when the task is administered during the stressor exposure, task performance is generally not affected by unpredictable events. Matthews et al. (1980) found that unpredictable noise was associated with slower reaction time. However, Carter and Beh (1987) did not find differences in performance on a vigilance task administered during regular or irregular noise bursts. In this study only the group that had irregular noise intervals and noise duration had greater error rates. This finding was not replicated in a similar study conducted by the same authors (Carter & Beh, 1989), and Grabitz and Wittmann (1986) reported no effects of loss or gain of predictability on performance on a simple arithmetic task.

When the task is administered after the stressor period, marked aftereffects on task performance and frustration tolerance appear. Glass and Singer (1972) conducted a series of

studies showing that predictable and unpredictable noise and shock can have different aftereffects. They gave subjects a series of simple tasks to work on while exposing them to either variable or regular intermittent noise at 56 or 108 dBA. Following the session subjects were given the Feather task (Feather, 1961) as a measure of frustration tolerance and a proofreading task in which they were instructed to find errors. Frustration tolerance, as measured by time spent on an unsolvable Figure of the Feather task, as well as proofreading performance were significantly higher in the groups exposed to predictable noise than in the unpredictable noise groups. Predictability was more important in determining outcomes than was the intensity of the noise. These findings were replicated using signaled vs. unsignaled noise.

In a similar vein, Mills and Krantz (1979) exposed 44 subjects to a cold pressor task and varied the amount of information given about possible sensations the task would induce. Subjects given sensory information, i.e. who could predict how they would react to the stressor, performed better on a subsequent proofreading task than those who were given no information. Another study examined the effects of information about experimental procedures on a frustration tolerance task following random 95 dBA noise bursts, but found that information had an adverse aftereffect on frustration tolerance with subjects in the no information group showing better results (Klein, Harris, & Michie, 1982). Self-report measures, however, suggested that the manipulation did not work as expected.

In sum, unpredictability has not been shown to have effects on task performance during the stressor but its negative aftereffects on performance as well as frustration tolerance seem to be reliable.

Physiological effects

The stressfulness of an event is often reflected in the magnitude of the physiological

response it elicits. Different stressors have been shown to cause changes in numerous physiological parameters including heart rate (HR), blood pressure (BP), galvanic skin response (GSR), catecholamines, and cortisol. Research on the effects of predictable vs. unpredictable stressors on physiological changes has been abundant, but most human research in this area has been done measuring GSR and HR. No laboratory studies assessing human endocrine changes could be found. Animal studies, on the other hand, have reported on a variety of physiological and health changes, including weight changes, gastric ulceration, and corticosterone level changes. These findings are often contradictory. Several studies have found that unpredictable aversive stimulation (e.g. shock) induces greater weight loss than predictable shock (e.g. Price, 1972; Weiss, 1970), while others report opposite results (Brady, Thornton, & DeFisher, 1962; Friedman & Ader, 1965; Pare, 1964) or no differences (e.g. Mezinskis, Gliner, & Shemberg, 1971). Data on gastric ulceration is more consistent and most agree that unpredictable shock is associated with more ulcers than predictable shock (Seligman, 1968; Seligman & Meyer, 1970; Weiss, 1970; Weiss, 1971). Plasma corticosterone and catecholamine levels have not been as responsive to predictability manipulations. One study found that predictable noise was associated with faster habituation of corticosterone levels than unpredictable noise in rats but reported no significant effects on catecholamine levels (DeBoer, van der Gugten, & Slangen, 1989). Other studies indicated that predictable shock evokes higher corticosterone levels (Bassett, Cairncross, & King, 1973; Davis & Levine, 1982; Experiment 3) or report no significant effects at all (Davis et al., 1982; Dess, Linwick, Patterson, Overmier, & Levine, 1983; Lawler, Cox, Barker, Hubbard, & Sanders, 1984; Mormede, Dantzer, Michaud, Kelley, & Le Moal, 1988).

Skin conductance and heart rate are by far the most frequently used measures in human predictability studies. The most popular experimental paradigm for this purpose manipulates predictability by the presence or absence of a warning signal before the aversive event. Katz

(1984) used a within subjects design, presenting subjects with 12 alternating signaled or unsignaled shock trials. There were no significant differences in GSR during the anticipatory period, even though subjects were informed about the predictability condition at the beginning of each trial. The unpredictable trials, however, were associated with a significantly greater magnitude of the response to the shock (1.5-4 sec. post-impact), but when change from trial onset was calculated the differences between the predictable and unpredictable trials were only marginal. In another study Lykken et al. (1972) varied the predictability of the timing and locus (which limb would be shocked) of the shock in 48 trials. When the shock was preceded by a signal both GSR and HR were significantly lower at shock impact than when the shock onset was unpredictable. Analyses were done by calculating the differences between values at shock onset and peak values after shock. No statistics were reported for anticipatory responses but the data show increases in HR and GSR in response to the signal. Information about the locus of shock had no significant effects on physiological responses.

Maltzman and Wolff (1970) exposed 40 subjects to alternating blocks of five trials of signaled delayed and signaled immediate 110 dBA white noise. After each signal subjects were informed that the noise would occur 'now' or 'later', the delayed condition being less predictable. Mean GSR levels were significantly lower in the immediate noise condition and this was due to faster habituation over time. A study on coronary patients and high and low coronary risk subjects examined the effects of 10 alternating trials of signaled and unsignaled 115 dBA noise (van Doornen, Orlebeke, & Somsen, 1980). A clock counted down the 12 seconds between the signal and the noise, assuring maximal predictability. All subjects' GSR levels were higher in response to the unsignaled than to the signaled noise although no statistics were reported. The differences between the signaled and unsignaled responses were significantly greater for the low risk group than for the high risk group and the patients. No significant differences were found

in anticipatory GSR. In the signaled conditions HR responses were significantly lower immediately after the noise but showed a greater acceleration over time than in the unsignaled conditions. Anticipatory HR responses, especially in the low risk subjects, were initially lower in the signaled condition where it progressively accelerated until noise onset, whereas in the unsignaled conditions anticipatory HR stayed relatively low. The data suggest that unsignaled noise responses are more stable whereas signaled conditions elicit great fluctuations in both HR and GSR.

One study examined effects of predictability on reactions during a relatively long anticipation period (Gaebelein, Taylor, & Borden, 1974). Subjects were told that they would receive shock after a waiting period of six minutes and half of them were given a clock counting down the six minutes (high predictability). The unpredictable group had no time cue (low predictability) and exhibited greater HR and SC increases to the actual shock. During the anticipatory period, however, very little difference between groups was detected with the exception of a HR increase one minute before shock in the predictable group which was not seen in the unpredictable group.

Monat et al. (1972) in two separate experiments monitored the time course of the anticipatory HR and GSR responses in conditions of temporal certainty and uncertainty in a between groups design. Male subjects were either told that they would receive shock anytime over the next 6 minutes (temporal uncertainty), or at the end of three minutes with a clock counting down to the occurrence of shock (temporal certainty). Shock was administered at the end of three minutes in all groups. In the certainty groups the perceived probability of shock was varied (100, 50, or 5% probability of shock). While the probability manipulation had no significant effects, the temporal uncertainty group differed from the certainty groups by the time course of their anticipatory responses. After an initial increase in HR and skin conductance (SC)

their levels gradually decreased over the course of the three minutes, whereas in the certainty groups arousal increased immediately before the shock. In the second experiment it was noted that the temporal uncertainty group had the highest average SC and GSR of all groups. This was not found in the first study. Klemp and Rodin (1976) varied the delay between a signal and shock (5 or 20 sec.) and gave the predictability group a clock counting down to the next shock. The unpredictability group (no clock) showed a significantly greater decrease in anticipatory HR than the predictability group. This was interpreted in terms of an orientation response (Lacey, Kagan, Lacey, & Moss, 1963) but, alternatively, could be also due to a lack of knowledge of when the shock would occur. No data on early anticipatory HR and response to the impact of the shock were reported, so no conclusions can be drawn.

Peeke and Grings (1968) administered shock to three groups of subjects which were differentiated by the predictability value of a warning signal they received. The ISI was either held constant at 5.5 seconds (high predictability), varied from .6 to 11 seconds (low predictability), or presented randomly during the session (no predictability). The GSR in response to the shock was significantly different among the three groups with the high predictability showing the lowest and the no predictability group having the highest response. This was mostly due to rapid habituation in the high predictability group and the absence of habituation in the no predictability group. Anticipatory responses to the signal were highest in the high and low predictability groups and differed significantly from the third group. Vila and Fernandez (1989) added extensive procedural information to their manipulation of temporal predictability of noise. Three groups were subjected to three trials of 109 dB noise bursts every 90 seconds. The noise was preceded by a ten-second signal for two of the groups, one of which in addition received detailed information about the experimental manipulation (information + predictability). Subjects' HR and GSR to the noise were significantly different with the

information + predictability group showing the lowest response and the no-predictability group the highest. This was mostly evident on the first trial, because all groups showed quick habituation for the remaining trials which was probably due to the regular interval at which the noise bursts occurred, making the event somewhat predictable for all groups. There were no differences in anticipatory responses among the groups.

Another way of varying the effectiveness of a warning signal is to vary its degree of ambiguity. Sosnowski (1988) asked subjects to compare the size of two circles presented on slides and told them that noise would occur when the second circle was larger than the first. In the unambiguous condition the two circles were always clearly different making it easy to predict the noise. In the ambiguous condition the two circles were always the same size and noise would occur on some trials and not others. Subjects' SC and HR changes overall were significantly higher for the ambiguous condition than for the unambiguous condition during the noise trials. For HR this was mostly due to differences in anticipatory responses, whereas SC responses were markedly different during both anticipatory and post-noise periods. These findings differ from the previous studies in that both predictability and unpredictability caused increased anticipatory responding in this study. The discrepancy may be due to the fact that both groups obtained a signal and the ambiguous group probably spent a lot of effort trying to discern its meaning.

The majority of studies have examined effects of painful physical or auditory stimuli, but predictability effects can also be obtained using different stressful events. This was explored by Price and Geer (1972) who used color slides of dead bodies which were preceded by a signal in half of the subjects. Spontaneous fluctuations (SF) of skin resistance were more frequent in the unpredictable group during the intertrial intervals. Further, GSR to the slides was higher in that group immediately (0-4 sec.) after onset of the aversive stimulus.

Several studies using signals to manipulate predictability found no significant

physiological effects. Glass and Singer (1972) exposed subjects to 25 minutes of intermittent noise that was either preceded by a signal, or was unpredictable because either no signal was present or the signal was not correlated with the noise. Although SC responses looked higher in the two unpredictable groups the differences were not statistically significant. Furedy and colleagues (1971, 1973) conducted two studies comparing signaled and unsignaled shock conditions and found no significant effects on GSR. Self-report data showed no significant effects of predictability on the perceived aversiveness of the shocks which suggests that the predictability manipulation had no effect in these studies.

Some of the studies reviewed earlier that provided subjects with a choice between vigilant (e.g. listening to a signal) or distracting (e.g. listening to music) coping strategies have also monitored their physiological responses. In this case, however, since subjects choose the experimental condition, there is a self-selection bias that limits interpretation of the results, especially since it has been suggested that certain personality traits may be associated with the choices made (e.g. Evans & Moran, 1987; Miller, 1981). Four studies fall into this category and their results will be briefly reviewed. In the study by Averill and Rosenn (1972) subjects who listened to warning signals predicting avoidable or unavoidable high intensity shock had significantly lower anticipatory SC levels than those who chose distracting music for more than 50% of the time. Vigilant subjects also had lower anticipatory HR levels than non-vigilant subjects in the low-intensity shock condition. Averill and colleagues in 1977 also found vigilant subjects to be less aroused than non-vigilant subjects in terms of anticipatory skin conductance and HR when shock was 100% avoidable. However, when shock was not avoidable vigilance did not affect physiological arousal. By contrast, Miller's (1979) data show that vigilant subjects were more aroused according to SC levels than those who chose distracting music. Finally, a study offering subjects a choice of information about what kind of stimulus they would receive,

reported no significant effects of information seeking on GSR (Lanzetta et al., 1966).

A few studies examined the effects of predictability by varying the regularity of presentation of the aversive stimuli. Lovibond (1968) administered electric shock at either regular (predictable) or irregular (unpredictable) intervals to two groups of female students. Subjects' GSR showed very little habituation in the unpredictable group when compared to the rapid habituation seen in the predictable group. Carter and Beh (1989) had subjects work on a vigilance task while they were listening to 92 dBA noise bursts that were presented at regular intervals and burst durations (predictable), at irregular intervals but regular durations (unpredictable 1), or at irregular intervals and durations (unpredictable 2). A fourth group was not exposed to the noise. Although the noise groups had significantly higher DBP and mean BP responses than the no-noise controls no significant effects were found for predictability. Subjects' HR responses, on the other hand, were significantly higher in the two unpredictable noise groups than in the no noise and the predictable noise groups. A similar study using continuous noise was reported by Linden (1987). Subjects were exposed to five minutes of either steady white noise, steady 'real-life' noise (background cafe noise), or variable 'real-life' noise (variable sounds of uneven durations, e.g. street noise, trains, etc.). All groups, including a no-noise control group, worked on a mental arithmetic task during that time. No significant BP differences were found between the groups, but HR responses were significantly higher for the variable noise group than any other groups. The results are confounded by the fact that in addition to varying predictability, the authors also varied the type of noise among groups. The differences in responses could be a result of a difference in the meaningfulness of the noises rather than level of predictability.

Glass and Singer (1972) also used a similar paradigm by changing the regularity of the

interstimulus intervals to manipulate predictability. They reported significant predictability effects on GSR in two separate studies. In the first, three groups of subjects working on arithmetic tasks of varying difficulty listened to 25 minutes of either fixed intermittent 92 dBA noise bursts (predictable), bursts of random duration and interval (unpredictable 1), or bursts of random duration and interval and variable intensities (unpredictable 2). Skin conductance response was significantly higher in the second unpredictable noise group towards the end of the noise session, suggesting slower habituation in the high unpredictability condition. The second experiment used a 2 by 2 design exposing subjects to either fixed or variable intermittent noise and half of each group to short (51 sec) average interburst intervals and the other half to long (96 sec) interburst intervals. There were no significant GSR differences due to variability of the noise but average length of interburst intervals did have an effect. The long intervals were associated with an inhibition of habituation of skin conductance over time whereas short average intervals were associated with rapid habituation over the 25-minute session. It has been argued that long interstimulus intervals may be associated with greater unpredictability because of the greater difficulty of estimating the time elapsed since the last stimulus making prediction of the next stimulus less accurate.

Zeichner and his colleagues incorporated the predictable stimulus into a task their subjects were working on. Type A and B men and women were asked to play a video game in which the target was either presented at regular 90-second intervals (predictable) or at random intervals (unpredictable). No BP differences were observed. The unpredictable group had higher blood volume pulse changes whereas the predictable group reacted with greater HR changes. The data may be confounded by possible differences in activity and task effort that the groups engaged in as a result of the different task conditions imposed by the predictability of presentation of the target (Zeichner, Allen, Spiga, Rudd, & Brown, 1990).

Other studies using similar designs found no effects of predictability on physiological function, including several studies reported by Glass and Singer (1972). When the authors administered variable vs. constant intermittent noise without randomly varying noise intensity or duration to subjects working on various simple tasks, they did not find significant effects on SC responses between the groups. Weidner and Matthews (1978) gave their subjects arithmetic problems to solve while exposing them to four minutes of fixed or variable noise. Although the two noise conditions elicited significantly higher BP compared to no noise controls, level of predictability did not differentially affect BP or hand temperature. One drawback of this study is that the physiological measures were not taken continuously but only after the noise exposure was over.

Two studies that varied the level of probability of shock administration measured physiological arousal. Grings and Sukoneck (1971) included four conditions in their study in which probability of shock predicted by a signal was either 0, 25, 75, or 100% (the number of shocks given reflected the probability in each of the conditions). The orienting response to the signal and the anticipatory GSR rose significantly as a function of shock probability whereas the response to the actual shock decreased with increasing probability. The 25 and 75% conditions are thought to reflect low certainty, and 0 and 100% are associated with high certainty (the results did not include responses in the 0% condition). The data, however, are confounded by the differences in the actual number of shocks administered in each condition. Epstein and Roupenian (1970) varied expected probabilities of shock holding the actual number of shocks administered constant across conditions. Subjects were told that they had a 5, 50, or 100% chance of receiving shock and then were exposed to a no-shock and a shock trial. The group with the 5% shock expectation had the highest anticipatory SC and HR response in both trials. The 50% group also had high anticipatory HR levels compared to the 100% group. The SC

response to the shock was highest in the 5% condition and HR responses were highest in the 5 and 50% conditions. Although the 50% expectancy level was thought to produce the greatest amount of uncertainty, self-reports showed that the 5% level induced more subjective uncertainty than the 50% level, i.e. a 50% chance of receiving shock was high enough for subjects to expect shock all the time, whereas a 5% chance, though low, made subjects aware enough of the possibility of shock that they would worry about it more than expected. This could explain the high physiological arousal seen in the 5% expectancy group.

In sum, while animal studies seem to find little consensus as to whether predictable or unpredictable stressors produce higher physiological arousal, most human studies converge on the conclusion that unpredictable aversive stimuli heightens at least one aspect of physiological responses. It appears useful to separate anticipatory responses from impact responsiveness since some data show a discrepancy between them. Several studies have found that while predictable stressors tend to increase anticipatory arousal, unpredictable stressors are associated with greater impact arousal. However, there is some variability in findings due to inconsistencies in experimental paradigms and choices of how the individual responses were defined. Further, this literature is limited by the measures used. GSR and HR are not sufficient indices of physiological arousal and use of a wider range of measurements including BP and hormonal measures would be useful (Baum, Grunberg, & Singer, 1982; Dimsdale, 1987).

Immunological changes

Only one animal study could be found that examined the effects of predictability on immune function. Mormede and colleagues (1988) administered intermittent shock at variable intervals to two groups of rats. In one group, shock was consistently preceded by a warning signal whereas in the other group the same signal was randomly presented during the session

without temporal association to the shock. A third group served as a no-shock control. Mitogenic responsiveness of splenocytes to concanavalin A (ConA) was significantly lower in the unpredictable group then the predictable and control groups, and the same trend was shown for phytohemagglutinin (PHA) and pokeweed mitogen (PWM) responsiveness although these differences were not significant. These immune changes were observed despite a lack of differential corticosterone responsiveness to the predictability manipulation suggesting that mechanisms other then the HPA axis may be responsible for the effect. To date, no human studies have been conducted this area. However, the data from the study by Mormede and colleagues suggest that examination of the mediating effects of predictability in stress-induced immunomodulation is a worthwhile and interesting area to be explored.

Conclusions

To briefly summarize findings from the literature, predictable stressors appear to be less stressful than unpredictable ones when indices such as preference, aversiveness ratings, self-reported distress, frustration tolerance and performance aftereffects, and physiological impact are considered. These data mirror the beneficial effects of information seen in field studies. Unfortunately, as in many research areas, the findings are not as clear as one would hope. Predictability has not always had the expected effects and some studies do not report evidence that predictability moderates the stressful impact of aversive events. One factor contributing to the discrepancy is the diversity of predictability manipulations, aversive stimuli, and subject samples used in the laboratory studies. Another problem is related to the difficulty in replicating real-life uncertainty situations in the laboratory. Although a laboratory paradigm is desirable for the sake of separating predictability from controllability issues, it is difficult to simulate a meaningful stressful event for which the presence or absence of predictability or information

would make a difference. Despite these limitations laboratory experiments are essential in determining mediating factors of stress and mechanisms by which they operate in alleviating the potentially devastating psychological and health effects stressors can entail in real life situations.

Summary and hypotheses

Research in naturalistic settings has shown that providing people with information about future events can have beneficial effects on their physical and mental health (e.g. Schulz, 1976). In laboratory studies, when subjects are given a choice between predictable and unpredictable aversive stimulation, most prefer the predictable condition (e.g. Lanzetta and Driscoll, 1966; Pervin, 1963). Further, predictable aversive stimulation appears to be less stressful than unpredictable stimulation as measured by self-report and psychophysiological indices, as well as aftereffects on performance (Glass & Singer, 1972; Katz, 1984; Weidner and Matthews, 1978). Despite several decades of research, however, a number of issues remain unresolved, including questions concerning the impact of predictability on underlying hormonal changes and possible immunologic mediation between predictability and health. Although physiologic and immunologic effects of predictability and controllability of a stressor have received ample research interest in the animal literature, little is known about how these factors mediate stress-induced physiological changes in humans.

The findings of psychoneuroimmunologic studies clearly demonstrate that stress can have effects on immune function, and that stress-hormones that are known to be sensitive to stress-reducing factors such as coping and perceived control play a crucial role in effecting these immune changes. Although, endocrine responsiveness to predictability manipulations has not yet been examined, the changes in HR and GSR that have been observed are likely to be a reflection of underlying systemic hormonal changes, that include fluctuations of the same hormonal changes

that are thought to affect the immune system in situations of stress. Moreover, a related concept, perceived instrumental control, has been extensively researched in terms of its endocrine effects in animals and humans and its immunological effects in animals. One study also found lack of control to be associated with immunosuppression in human subjects (Sieber et al., 1992). Finally, one animal study succeeded in showing that an unpredictable stressor has greater immunosuppressive effects than a predictable one (Mormede et al., 1988).

The present study used the findings from the stress and psychoneuroimmunology literature to examine how predictability affects the stressfulness of an aversive stimulus. The study incorporated multiple measures of stress including cardiovascular, self-report and behavioral, and examined whether stress-induced immune changes would be sensitive to the mediating effects of this psychological variable. This research was conducted in a controlled laboratory setting, in order to be able to establish causal relationships, to rule out factors that can affect endocrine and immune function that usually accompany stress in a naturalistic setting, and finally, to examine the effects of predictability alone without the confound of actual instrumental control that usually interferes in field studies. Although, naturalistic stressors are usually more potent and meaningful, laboratory stressors have been shown to reliably induce psychological, endocrine and immunologic changes and can be used as a model for a study examining the effects of cognitive mediators on these changes.

In order to examine the contribution of predictability to the stress-related psychological, cardiovascular, and immunomodulatory effects seen in previous research, a standard laboratory stressor, the cold pressor task, was used. This task was chosen for several reasons. The cold pressor test has well-known cardiovascular and psychological effects as it has received extensive prior psychophysiological research (Lovallo, 1975). Although, the cold pressor task is different from other stressors used in acute PNI research because it is a physical stressor as well as a

psychological one and involves cold and pain sensations, the known cardiovascular and endocrine effects of this stressor lead one to believe that it would have similar effects on immunity by way of the sympathetic nervous system and the hypothalamo-pituitary-adrenal axis as the stressors used in previous research. In support of that idea, animal studies have shown that cold stressors can reduce immune function such as lymphocyte proliferation and natural killer cell activity (Jiang, Morrow-Tesch, Beller, Levy, & Black, 1990). Further, in order to continue to test the reliability of this laboratory model in producing immune changes, it is necessary to assess the immunomodulatory effects of various types of standard laboratory tasks. Finally, this stressor was chosen for practical purposes. In order to be able to manipulate predictability of the stressor duration an intermittent and repetitive task was required. Frequently, a noise stressor has been used for this purpose but a more stressful stimulus was necessary for eliciting immunological changes.

Predictability in this study was manipulated by varying the amount of information about one aspect of the task. Previous problems encountered in laboratory studies examining the effects of perceived control on immunity (Sieber et al., 1992; Weisse et al., 1990) were eliminated from this study because no overt activity was involved in the predictability manipulation that would be comparable to the button pressing response to control an aversive stimulus. A multi-level measurement approach was used to assess the effectiveness of the stressor and the predictability manipulations.

The following hypotheses were addressed in the proposed study:

1. a. Human subjects exposed to several trials of a painful cold pressor task will exhibit increases in BP and HR, self-reported moods and symptoms associated with stress, and reduced frustration tolerance post-task when compared to subjects not exposed to the stressor.

b. Information about the duration of the cold pressor trials (predictability) will significantly

attenuate the stressfulness of the task and therefore reduce the psychological, physiological, and behavioral signs of distress associated with it.

2. a. The immune changes found in response to acute stressors in previous research will be generalizable to a different type of standard laboratory stressor involving psychological distress as well as physical sensations of cold and pain. The cold pressor task should therefore evoke reductions in lymphocyte responsiveness to mitogenic challenge.

b. The stress-moderating effects of the predictability manipulation will be reflected in attenuation of the stress-related reductions in lymphocyte proliferation such that the predictable stressor will have less of an impact on blastogenesis than the unpredictable stressor.

Methods

Overview

This study examined the stress-mediating effects of predictability on psychological, behavioral, physiological, and immunological function by using a laboratory stressor consisting of a cold pressor task. Three groups were included in this design, a no stress control group, and two stress groups one of which was given information predicting the duration of each of ten cold pressor trials (predictable), and one in which that information was omitted (unpredictable).

Subjects

Participants were 36 healthy male volunteers between the ages of 18 to 45, recruited through local newspaper advertisements. The number of subjects was determined based on previous studies on acute stress and immune function that showed that 12 subjects per group were sufficient to generate significant effects. This number was confirmed by power analysis based on data from a previous study (Zakowski, et al., 1992). Analyses of these data showed that effects of stress on lymphocyte proliferation are greatest 15 minutes after beginning of the stressor. Means and standard deviations were calculated for lymphocyte proliferation during that time point and used to calculate an average effect size of .53 according to standard statistical procedures (Cohen, 1988). Using an alpha level of .05 and a power level of .80, 12 subjects per group were required for this study.

All volunteers were screened by telephone using a standardized script (see appendix A). They were asked questions pertaining to their history of drug use and physical and mental health, which included a list of health problems and disorders (e.g. hypertension, cancer, diabetes,

allergies, ulcer, etc.) that they were to identify if any applied to them. Individuals were recruited if they met the following criteria: no chronic health problems (including circulatory problems and Raynaud's disease), no medication use, no nicotine or drug use, no excessive caffeine or alcohol use (i.e. more than six cups of coffee or more than three drinks per day), and no psychological problems requiring treatment. These criteria were established in previous studies in our laboratory in order to exclude any extraneous factors that could potentially affect physiological reactivity and immune function changes.

Design

Subjects were randomly assigned to one of three groups: a no-stress control condition (NS) which served to control for the effects of blood drawing procedures and circadian variations in physiological measures (Tavadia, Fleming, Hume, & Simpson, 1975), a predictable stressor condition (PR), and an unpredictable stressor condition (UPR). Within each group repeated measures were taken in order to assess self-report, cardiovascular, and immune changes over time. Therefore, the stress manipulation constituted the between subjects factor and the repeated measures the within subjects factor. Several questionnaires were administered to measure background stress levels. Finally, all subjects completed the Feather task (Feather, 1961) at the end of the session as another way of assessing the effectiveness of the manipulation by examining whether the adverse aftereffects of unpredictability on frustration tolerance could be replicated (see Glass & Singer, 1972).

Procedures

The laboratory sessions were started between seven and nine o'clock in the morning and took approximately 2.5 hours. Subjects were asked to refrain from any foods high in fat or

cholesterol content (e.g. eggs, butter, whole milk, bacon, etc.) the morning of the session because of their potential effects on the blood and were asked not to drink more than two cups of coffee the day of the session. Compliance with these instructions was later verified using questionnaires (see below). Also, since subjects were required to be healthy in order to meet study criteria, they were rescheduled in case of any acute illnesses (e.g. cold or flu) occurring within two days prior to the session. Upon arrival at the laboratory the procedures were explained briefly as follows:

"We are interested in measuring your physiological responses to various tasks. We have included several groups in this study, each of which will be given different tasks. I will ask you to work on one of the tasks which I will explain to you in a few minutes. In addition to the task I will give you questionnaires asking about background information and your reactions to the tasks. The session will take about two and a half hours and you will be paid $ 30 in the end. The tasks themselves will only take about 20 minutes. The rest of the time you will fill out questionnaires or relax. In order to measure HR and BP I will put this BP cuff on your dominant arm. The cuff will inflate automatically every few minutes before and during the task. In addition, I will attach three electrodes to your chest which will measure your heart rate. Further, for the purpose of measuring immune function I will take several blood samples during the session. I will take one sample before the task, one during and two after the task. I will do this with a small butterfly needle that will stay in your forearm vein for the entire session. Do you have any questions?"

After this initial description informed consent was obtained and the first three baseline BP and HR readings were taken in order to obtain resting cardiovascular measures before any blood drawing procedures were started. Then, the intravenous catheter (a 19-gauge butterfly needle) was inserted into the subject's antecubital fossa and the first blood sample was taken for baseline immune assessment. Periodic infusions of 1 ml of Heparin (100 units/ml) after every

blood draw ensured patency of the catheter. The subject was instructed to rest for another 20 minutes in order to allow for recovery from the blood drawing procedures before beginning of the tasks. During this time, five additional resting HR and BP measures were taken, the last three of which constituted the actual resting baseline measures used in the data analyses.

The laboratory tasks were explained to the PR and UPR groups as follows:

"In a few minutes we will be ready to start the task. The task you are going to complete is a cold pressor test. That is, for the next 20 minutes I will periodically ask you to immerse your dominant hand into a basin of cold water for variable amounts of time. You are to put your hand all the way into the water without touching the bottom of the basin until I tell you to take it out. If you do take your hand out earlier we will have to stop the experiment because we will not be able to use your data. Before we begin the task I will start a tape that will provide you with instructions throughout the task. Please pay close attention to these instructions."

The NS group was given similar instructions except that they were told that they would put their hand in luke warm water. Subjects underwent exactly the same procedures as the PR group except that instead of the cold water they were only exposed to body temperature (35-37°C) water. This procedure was included in order to control for activity and effects of the blood drawing procedures in the least stressful manner possible.

Following this introduction, subjects listened to a tape that gave more detailed instructions and provided them with information throughout the task. It was the amount of information provided on the tape that determined the predictability or unpredictability of the trial durations.

Each trial lasted between 17 and 75 seconds and was administered at 60-second intervals. A second blood sample was taken ten minutes into the task, after the first five trials, in order to assess early effects of the stressor on immune function. Previous research has shown that the greatest immune effects resulting from an acute laboratory stressor occur 10 to 20 minutes within

Subsequently, subjects completed another 5-trial set of the task lasting another ten minutes. A third blood sample was drawn at the end of the task. Subjects were asked to rate their pain and distress in response to four out of the ten cold/warm pressor trials, i.e. after the second, fifth, seventh, and ninth trials. Further, mood ratings were obtained after each of the two ten-minute task periods. A questionnaire assessing perceived control and predictability was administered immediately after the last task period. After a 20-minute rest period the fourth blood sample was taken in order to be able to track the timecourse of the immune changes and to pick up potential delayed immune effects in response to the stressor. The catheter was removed immediately following this last blood draw. Finally, the Feather task was administered. At the conclusion of the task the subject was debriefed and paid.

To summarize, these procedures are presented in the timeline below:

Time (min.)		Measures
-15	Informed consent	
0	Rest (15 min)	BP, HR (3)
15	Blood draw #1	Immune measures
20	Rest (20 min)	BP, HR (5), mood
40	Task 1 (10 min)	BP, HR (5), pain, distress
50	Blood draw #2	Immune measures, mood
55	Task 2 (10 min)	BP, HR (5), pain, distress
65	Blood draw #3	Immune measures, mood
70	Rest (20 min)	Predictability ratings
90	Blood draw #4	Immune measures
95	Feather task	
	Debriefing	

Cold pressor task

The cold pressor task was used because several studies have shown its effectiveness as a stressor in eliciting psychological, physiological, and behavioral responsiveness (e.g. Lovallo, 1975; Mills et al., 1979; Street, et al., 1984). Increases in DBP, norepinephrine, and vasoconstriction have been observed in response to the cold pressor task all of which are related to sympathetic nervous system (SNS) activity. Sympathetic activity, in turn, is thought to underly stress-induced immune changes. It therefore seemed reasonable to believe that this task would elicit similar immune response changes as other sympathetically activating laboratory stressors that have been used in previous immune studies. Finally, the intermittent nature of this task allowed for the manipulation of predictability much more readily than any other more continuous type of stressor.

The water temperature was set at 5-6°C for the cold pressor and at body temperature for the warm water (35-37°C). Each trial lasted 17 to 75 seconds (the duration of each trial varied randomly) and the intertrial intervals were one minute each for all three groups. The intertrial intervals were chosen in order to allow subjects to recover from each cold pressor trial so as to avoid rapid habituation to the cold which is more likely to happen when the intervals are shorter and the subject's hand is constantly cold. In addition, the 60-second intervals allowed enough time for the self-report and cardiovascular measures taken in between trials. The cold/warm pressor trials were presented for 17, 74, 55, 27, 69, 50, 34, 18, 75, 63 seconds for the respective trials. A five minute break after the first set of five trials allowed time for administration of questionnaires and obtaining of blood samples.

Predictability manipulation

Predictability of the duration of each trial was manipulated. Since the duration of the

cold/warm pressor trials varied randomly from 17 to 75 seconds subjects were unable to predict the duration of each trial if they were not given further information. Subjects in the PR and NS groups listened to a tape that provided them with information as to the duration of each trial by telling them at the beginning of each trial how many seconds that trial would last and then counting down to 0 seconds during each of the trials. This gave subjects constant feed-back on how much longer they would have to keep their hand in the water. The taped instructions for the NS and PR groups were as follows:

"The following task is designed to measure your physiological reactions. For the next 20 minutes you will be asked to periodically put your hand in a basin filled with water by immersing your hand in the water up to your wrist without touching the bottom of the basin. Whenever I say the word "start", you are to put your hand in the water basin until I tell you to stop. When I say "stop" you are to take your hand out of the water. Every time I say "start" I will also tell you how many seconds your hand should remain in the water, and I will count down to 0 seconds at which point I will say "stop" and you will remove your hand from the water. For example I may say "start, 4 seconds, 3, 2, 1, 0, stop". The amount of time you will have to keep your hand in the water will vary for every trial. Throughout this test it is very important that you do not take your hand out of the water before I say stop! If you have any questions you may ask them now."

The US group listened to a similar tape but received no information as to the duration of each trial. Instead of listening to the count down they were exposed to the same voice repeating random numbers. This was done to control for the possible effects of distraction of the predictability manipulation by ensuring that all subjects were exposed to the same amount of external stimuli:

"The following task is designed to measure your physiological reactions. For the next

20 minutes you will be asked to periodically put your hand in a basin filled with water by immersing your hand in the water up to your wrist without touching the bottom of the basin. Whenever I say the word "start", you are to put your hand in the water basin until I tell you to stop. When I say "stop" you are to take your hand out of the water. Every time I say "start" you will also hear random numbers repeated on the tape. For example I may say "start, 3, 8, 2, 6, stop." These numbers are recorded in order to drown out static noise on the tape and have no meaning whatsoever for the task. The amount of time you will have to keep your hand in the water will vary for every trial. Throughout this test it is very important that you do not take your hand out of the water before I say stop! If you have any questions you may ask them now."

Following this information, the ten cold pressor trials were administered prompted by instructions on the tape telling subjects when to start and end each trial. It should be noted that the NS group was given instructions that enhanced their predictability over the situation, therefore this is not a complete factorial design crossing predictability with stress. This control group was chosen in order to control for effects of venipuncture and circadian variations in the immune measures. The study therefore required control subjects to be exposed to the least arousing or stressful situation possible. Further, examination of the effects of predictability in itself over a non-stressful event was not one of the goals of this study and for that reason it was not necessary to include an unpredictable control group.

Measures

Measures of predictability

A questionnaire designed specifically for this study was administered at the end of the second task period to assess the effectiveness of the predictability manipulation. Two questions asked subjects to rate how predictable they felt the duration of the cold/warm pressor trials were,

and one question asked about their desire for predictability. In order to make sure that there was no unintentional carryover effect of the predictability manipulation to other aspects of the stressor, subjects were also asked to rate whether they thought that the duration of the following trials could be easily predicted. The ratings to this question were expected to be low in all conditions because no part of the instructions should have enhanced the predictability of this aspect of the manipulation since all trials randomly varied in their duration. Subjects also rated the amount of control they experienced during the tasks in order to address a possible relationship between predictability and perceived control. Finally, the questionnaire also contained a checklist of certain coping behaviors that subjects may have engaged in to deal with the stressfulness of the task. This list was designed after Miller's Behavioral Style questionnaire to examine potential individual differences in monitoring vs. blunting behaviors in response to this particular laboratory task. These are side issues in this study and due to lack of standardization and psychometric data on this questionnaire, the data obtained from these items can be used as pilot data at best. No standardized questionnaires could be found in the existing literature that addressed these issues.

Measures of stress

Stress was assessed at two levels. First, self-report, cardiovascular and behavioral measures served as the main dependent variables to address the first experimental hypothesis assessing (a) whether the cold pressor task was stressful and (b) whether predictability attenuated the stressfulness of the task. Other measures were taken in the form of questionnaires to examine the possible presence of extraneous sources of stress that might affect subjects' reactions to the manipulation.

Measures of the stressfulness of the tasks. The effectiveness of the manipulations were assessed using self-report, performance, and cardiovascular measures, in order to obtain a more complete picture of the extent of the subjects' reactions. The stressfulness of the manipulation was assessed with a 24-item stress scale that has previously been shown to distinguish effectively between stressor and control conditions (Zakowski et al., 1992). Subjects were asked to rate the extent to which they experienced different stress-related feelings on a five-point scale ranging from 'not at all' to 'extremely'. This questionnaire was administered three times during the session: at baseline, after the first 10-minute task period and at the end of the second task period.

A rating scale specifically assessing subjects' reactions to the cold pressor (i.e. pain and distress ratings) was given immediately after four of the ten cold/warm pressor trials (trials 2, 5, 7, and 9). This was a brief form which required subjects to indicate a number indicating how much pain and distress they experienced. An additional question assessing overall distress experienced in response to the task was incorporated into the questionnaire assessing the effectiveness of the predictability manipulation (see above). Subjects had to rate on a seven point scale how stressed they were during the 20-minute task they had just completed.

In order to measure cardiovascular reactivity to the stressors, HR and BP were assessed using an ambulatory BP monitor (Accutracker, Suntech) calibrated to a mercury column. An automatically inflating BP cuff was put on the subject's dominant arm. Three chest leads were attached to measure HR. Readings were taken every two minutes at baseline and during the two ten-minute stressor periods.

The Feather task (Feather, 1961) was used to examine whether the stressor aftereffects on frustration tolerance shown by Glass and Singer (1972) could be replicated as another measure of the effectiveness of the manipulation. A shortened version of the one described by Glass and Singer (1972, page 48) was used for this study. The task consisted of several copies of cards

with two different line diagrams stacked in two piles face down in front of the subject. The subject was to trace the lines of the puzzle without lifting the pencil and without tracing any line twice. He was told that he had as many trials on each Figure as he wanted but that there was a time limit on how long he was allowed to work on each trial. After each trial the subject had to decide whether to take another copy of the same card or to go on to the second pile of cards. The first diagram that was given to the subject was unsolvable, whereas the second one was solvable. Frustration tolerance was measured by recording the number of trials taken for the unsolvable diagram.

Chronic stress. Background levels of stress were assessed using several inventories administered during rest periods before and after the tasks in order to control for ongoing stress that may affect the main dependent measures in this study. These questionnaires included the SCL-90R (Derogatis, 1977) which consists of a list of symptoms and subjects are asked to rate on a scale from 0 to 4 how much they have been bothered by each symptom in the past two weeks. The questionnaire yields nine subscales, including anxiety, depression, anger, somatic complaints, and phobic ideation. A modified version of the Recent Life Changes Questionnaire (Holmes & Rahe, 1967) was used since the number of life changes experienced has been related to levels of stress and occurrence of illnesses. Both the number of life events experienced in the past six months and the amount of adjustment required for each of the events is measured by this inventory. The Daily Hassles Scale (Lazarus & Cohen, 1977) lists a variety of minor everyday stressors that have been associated with chronic stress. Subjects indicate which hassles they have experienced in the past month and rate their severity on a three-point scale ranging from 'somewhat severe' to 'extremely severe'. Finally, the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), asked subjects to rate the frequency of 14 different feelings that they may

have had over the past month on a five-point scale ranging from 'never' to 'very often'.

Background measures

In order to control for other extraneous sources of variance and to be able to assess comparability of the three experimental groups several questionnaires were administered measuring demographics, nutritional variables, perceived control, and desire of control. Subjects completed a background questionnaire asking about income, age, marital status and other demographic variables and two measures attempting to control for food and vitamin intake listing different foods and asking about eating habits as well as alcohol and caffeine consumption. A questionnaire asking about exercise habits and various sources of stress experienced the day of the session was also included to account for any variance in dependent measures not due to the manipulation.

Perceived control and desire for control were assessed because they may affect the subject's reaction to the predictability manipulation. The Desire for Control Scale (Burger & Cooper, 1979) lists 32 items pertaining to control which subjects rate on a seven-point scale. Perceived control was measured with a brief questionnaire asking about control and social support (Fleming, Baum, Gisriel, & Gatchel, 1982).

Finally, as a measure of desire for predictability, the Miller Behavioral Style questionnaire classified subjects into 'monitors' versus 'blunters' according to their endorsements of different types of behaviors in response to four hypothetical case scenarios (Miller, 1987).

Immune measures

Two types of immune measures were taken by performing functional and quantitative in vitro assays. Immune function was assessed by lymphocyte proliferation responsiveness to

mitogenic challenge. Blood samples were collected in heparinized tubes. Lymphocytes were separated under sterile conditions by Ficoll-Hypaque sedimentation and adjusted to final concentrations of 2 x 10^6 mononuclear cells per ml of RPMI 1640 medium with Hepes supplemented with 2mM L-glutamine, 100 U/ml penicillin, 100 ug/ml streptomycin, 1mM sodium pyruvate, 0.1 mM non-essential amino acids, 5 x 10^{-5} M 2-mercaptoethanol, and 5% heat inactivated fetal calf serum. Concanavalin A (Con A, Sigma Medical Company, St. Louis, MO.) was used at working concentrations of 5 and 10 ug/ml and pokeweed mitogen (PWM, Sigma Medical Co.) at 0.1 and .01 ug/ml. Each assay was performed in triplicate. 100 ul of mitogens was added to 2 x 10^5 cells in 100 ul of complete RPMI in flat-bottom 96-well plates. After a 52-hour incubation period cell cultures were pulsed with tritiated thymidine. After an additional incubation of 18 hours the cultures were harvested onto glass fiber filter paper and counted in a liquid scintillation counter.

Two quantitative assays including white blood cell counts and cell differential counts yielding the percentage of lymphocytes, monocytes, and granulocytes were performed. Whole blood drawn into tubes prepared with EDTA was used for these assays.

Results

Overview

Before the major hypotheses could be tested, comparability among the three experimental groups had to be established on all of the major background measures, including recent life events, daily hassles, symptom reporting, desire for control, food consumption, etc. Further, baseline values for self-report, cardiovascular, and immune measures were compared among the groups. ANOVA or Chi-square analyses using each of these variables separately were done for this purpose.

In order to make sure that the manipulations were successful and to examine the first study hypotheses, comparing the stressfulness of the three tasks, the groups were compared on the various behavioral, psychological, and physiological measures. Repeated measures ANCOVA were performed, covarying for respective baseline values, on self-reported distress at two experimental time points, on the pain and distress ratings at four time points (i.e. after the second, fifth, seventh, and ninth cold/warm pressor trials), and on blood pressure and heart rate using means for the two ten-minute task periods. Baseline values were used as covariates in order to control for initial values. ANOVAs were done to evaluate group differences in frustration tolerance on the Feather task by using the number of trials on the unsolvable Figure as the dependent variable.

The second pair of hypotheses, examining the effects of the stressor and predictability manipulations on the immunologic measures, were tested by comparing the three groups on the time course of their lymphocyte proliferation changes and changes in WBC and cell differentials. Repeated measures ANCOVA, covarying for baseline values, were used for this purpose. Immune function and status over the four experimental time points were analyzed for each of the

mitogens and cell subsets separately. Baseline values were used as covariates for the same reasons as stated above. In order to assess the contribution of BP and self-report measures of stress to the changes in blastogenesis, correlations between stress measures and proliferation change scores were conducted. All correlations were done within each condition because in light of the group differences in the measures of stress (see below) it was expected that different mechanisms were operating in each experimental condition and therefore different correlations were expected for each group.

Group comparability

Before examination of the major hypotheses, analyses established that there were no differences among the experimental groups on any of the demographic or background variables that could account for group differences in the major dependent variables. ANOVA and Chi-square analyses were conducted on the scores of all of the background measures described above. One subject in the PR group who had received a flu vaccine the week prior to participating in the study, had to be excluded from data analyses due to possible effects of the vaccine on the immune measures taken in this study.

The three groups did not significantly differ on any of the demographic variables. Subjects' ages ranged between 18 and 44 (M=29.4, SD=6.9). Race was evenly distributed across groups with 68.6% of subjects being Caucasian and 31.4% African American. Most subjects were single (57.1%), 34.3% were married, and a small percentage of volunteers were either divorced or widowed (2.9% and 5.7% respectively). The subjects ranged in height from 63 to 74 inches (M=70, SD=2.8) and in weight between 125 and 215 pounds (M=170.1, SD=20.8). The average income was $20,000-30,000 and average years of education was 16 years.

The groups did not differ on chronic stress measures, including number of recent life events, daily hassles, symptom ratings on the SCL-90-R, or overall perceived distress. Related mediating variables such as perceived control and social support as well as desire for control and monitoring/blunting behavior styles were also comparable among the groups. In addition to chronic stress levels subjects were also asked about stress and certain behaviors during the 24-hour period before the laboratory session. The groups did not differ in terms of number of stressors they expected to experience the day of the session, amount of sleep the night before the session, number of hours of exercise in the last 24 hours, how much coffee or alcohol they had consumed, or how well they felt overall the day of the session.

None of the subjects had any chronic or current health problems and in addition there were no significant differences between the groups in terms of number of health problems in the past or ratings of overall well-being in the present. Finally, the experimental groups had comparable baseline levels of all dependent measures including self-reported moods and symptoms of distress, BP and HR, cell counts, and lymphocyte proliferation to Con A and PWM.

Manipulation check of predictability

One questionnaire designed specifically for this study included two questions assessing whether the predictability manipulation was effective. ANOVAs comparing the three groups on their predictability ratings were conducted. For the question "During each trial were you able to predict when it (the trial) would end" the analysis yielded a significant group effect, $F(2,34)=13.68$, $p<.0001$, with the UPR group having significantly lower scores than the PR and NS groups (Tukey, $p<.05$). For the question "Did the numbers on the tape help you judge how long each trial would last?" the UPR group also had the lowest ratings, $F(2,34)=15.18$, $p<.0001$ (Tukey, $p<.05$) (see Figure 1). When asked about their preferences for predictability, there

were no significant differences among the groups. Another question asking "After each one of the trials, were you able to predict approximately how long the following trial would last?" was included in the questionnaire in order to ensure that there were no cues inadvertantly embedded in the manipulation that would give subjects information about the duration of the remaining trials. As expected there were no group differences in subjects' ratings to this question and the mean scores were very low (M=.33, 1.27, 1.17, for the NS, PR, and UPR groups respectively) suggesting that predictability was only manipulated for the duration of each individual trial. Finally, in an attempt to be able to separate effects of predictability and potential effects of perceived control, subjects were asked how much control they felt they had over the procedures. There were no significant differences among the groups suggesting that the predictability manipulation was not accompanied by a heightened sense of control over the task (M=3.5, 2.64, 1.83, for the NS, PR, and UPR groups respectively).

In sum, these results suggest that the information given to the PR and NS groups was successful in manipulating predictability of the duration of each individual cold/warm pressor trial that was not generalized to the rest of the procedures and that was not accompanied by a perceived control effect (see Table 2).

Measures of Stress

For the purposes of assessing whether the stressor manipulation was successful and to address the first hypothesis of differential stressfulness of the predictable and unpredictable stressors, repeated measures ANOVAs were performed on the various measures of stress including self-reports of pain, distress, and cardiovascular measures.

Self-report

Information on psychological distress in response to the tasks was drawn from three sources: the mood scale administered three times during the session, one question on the predictability questionnaire administered after the tasks, and the pain and distress ratings obtained immediately after four of the cold/warm pressor trials.

First, the mood scale was factor analyzed to yield three subscales: Negative affect encompassed 10 symptoms including terror, fear, restlessness, nervousness, tension, worry, helplessness, and feeling trapped, scared and shaky (Cronbach's alpha=.95); pleasant mood included feeling relaxed, comfortable, calm, pleasant, and at ease (Cronbach's alpha=.90); energy consisted of feeling energetic, confident, rested, and low in energy (Cronbach's alpha=.83). Several items were discarded from the questionnaire because they did not reliably cluster with any of the factors. The positive items were recoded so that a high score always signified high distress or negative mood, and a low score low distress or positive mood. Repeated measures ANCOVA were performed on each of the three subscales for the two timepoints of administration of the questionnaire, i.e., after each set of five cold/warm pressor trials. Baseline mood ratings were entered as a covariate. The groups differed significantly on their ratings of positive moods experienced during the task, $F(2,30)=4.31$, $p<.02$. Tukey post-hoc analyses revealed no significant group differences but there was a trend for the PR group to report lower positive affect after the second part of the task (see Tables 3 to 5).

One question on the predictability questionnaire asked "How stressed did you feel during the tasks?". Since no baseline measures were available for this questionnaire a simple ANOVA was done to show that the groups reacted differently to the tasks, $F(2,34)=10.39$, $p<.0001$, with the PR group reporting the greatest amount of distress (Tukey, $p<.05$) (see Table 2 and Figure 2).

Pain and distress ratings were obtained immediately after the second, fifth, seventh, and ninth cold/warm pressor trials and these ratings were entered into a repeated measures ANOVA. No baseline values were available for this measure. The groups differed significantly on their pain, $F(2,32)=55.71$, $p<.0001$, and distress ratings, $F(2,32)=27.68$, $p<.0001$. The group by time interaction effects were also significant for both variables, $F(6,58)=5.62$, $p<.0001$, $F(6,58)=2.31$, $p<.045$, respectively. The two stressor groups rated the task as significantly more painful and distressing than did controls. In addition the PR group reported more distress after the fifth and ninth trials and more pain after the ninth trial than either the UPR or the NS groups (Tukey, $p<.05$) (see Tables 6 and 7, Figures 3 and 4).

These self-report data showed that the cold pressor task was significantly more painful and distressing than the warm-pressor control task. However, contrary to initial expectations, the predictable stressor elicited higher ratings on the self-report scales, and this was true for pain and distress ratings of some trials and for overall perceived stress.

Cardiovascular measures

BP and HR readings were taken at four time periods during the study. Three readings were taken at the beginning of the session, before insertion of the catheter, five readings over a 20-minute rest period after insertion of the catheter, five readings during the first set of cold/warm pressor trials (first ten-minute task period), and another five readings during the second set of trials (second ten-minute task period). For the purpose of data analyses the mean of the last three resting readings before beginning of the tasks was calculated and this score constituted the baseline that was entered as a covariate into the repeated measures ANCOVA. As the main dependent measure in the ANCOVA the five readings for each of the two task periods were averaged and entered as two time points in the repeated measures design. Separate

ANCOVAs were run for each of the three cardiovascular measures, SBP, DBP, and HR.

SBP was significantly affected by the stress manipulation as evidenced by a significant group main effect, $F(2,31)=5.73$, $p<.008$, and a group by task period interaction, $F(2,32)=3.22$, $p<.05$. However, Tukey post-hoc analyses showed that only the UPR group was significantly greater than the NS group during the first task period, whereas the PR group was not significantly affected. During the second task period the groups were comparable suggesting habituation to the stressor (see Table 8, Figures 5 and 6). DBP showed similar effects. Repeated measures ANCOVA yielded a significant main effect for group, $F(2,31)=4.28$, $p<.02$, and a group by task period interaction, $F(2,32)=6.21$, $p<.005$. During the first task period both stressor groups had significantly elevated DBP readings (Tukey, $p<.05$), whereas all groups were comparable during the second task period (see Table 9, Figures 7 and 8). Finally, HR changes were analyzed and a significant group by task period interaction emerged, $F(2,32)=6.97$, $p<.003$. The PR group had the greatest HR elevations compared to the UPR group and controls (Tukey, $p<.05$) (see Table 10, Figures 9 and 10).

In the PR group SBP and DBP changes were highly correlated with self-reports of pain and distress. No significant correlations between HR and self-report variables were found. In the UPR group, however, far fewer significant correlations were found between self-report and cardiovascular changes, and the strength of these correlations was lower. While all correlations were positive, self-reported pain and HR were negatively correlated (see Table 11). Further, the cardiovascular measures were correlated with each other and it was found that there were fewer significant correlations in the UPR group and the magnitude of the correlations was usually lower than in the PR group. The stability over time of each of the cardiovascular measures was lower in the UPR group as well (see Table 12). When correlations were run among the ten SBP measures taken over time it was found that they were very inconsistent with some being positive,

negative, or non-significant.

In sum, these results indicate that the cold pressor task elicited significant increases in DBP regardless of predictability. Although, SBP elevations occurred in both stressor groups they were only significant in the UPR group, whereas HR elevations were only significant in the PR group.

Behavioral aftereffects

All subjects completed an unsolvable and a solvable puzzle of the Feather task approximately 25 to 30 minutes after the end of the cold/warm pressor tasks. The number of attempts at solving the first (unsolvable) puzzle were calculated and used as a measure of frustration tolerance. ANOVA yielded no significant differences among the groups, suggesting that the stressor had no significant aftereffects on frustration tolerance using this measure. The number of trials subjects took to complete the solvable puzzle also showed no significant group differences (see Table 13).

In summary, analyses of the various stress measures showed that the stressor manipulation was successful in eliciting predicted self-report and cardiovascular reactions. The first study hypotheses suggested that the cold pressor task would be stressful and that the predictable task would be less stressful than the unpredictable one. This was only partially confirmed. Although, the UPR group showed greater SBP responsiveness to the cold pressor task than either of the other groups, the PR group had the greatest HR elevations. It should be noted that these differences held primarily during the first task period. Self-report data suggested that the unpredictable stressor was less painful and less distressing.

Coping

In order to explain these discrepant results, coping styles used in response to the tasks were examined by assessing differences in the number of 'monitoring' vs. blunting' items checked on the last question of the predictability questionnaire. Data were coded according to the Miller Behavioral Style questionnaire method, i.e. the number of monitoring items were subtracted from the number of blunting items, so that a positive score means that the subject engaged in more blunting or distracting behaviors than in monitoring ones and vice versa. The following items were designated as distracting types of behaviors: "I tried to think about pleasant memories", "I tried to forget about the sensations in my hand", "I did not want to know how much longer I would have to keep my hand in the water", "I tried to tune out what was happening in the room", "I tried to relax". The remaining statements were put in the monitoring category: "I tried to focus on the sensations in my hand", "I tried to Figure out how much longer I would have to keep my hand in the water", "I thought about how I could get more information on how long the next trials would last", "I listened closely to the tape", "I looked around the room for clues to get more information about the task". This score was then analyzed using ANOVA. There was a marginal effect for this variable suggesting a trend towards a greater use of blunting or distraction types of behaviors in the UPR group compared to the PR group, $F(2,34)=2.46$, $p<.1$ ($M=.58$, .36, 1.67 for the NS, PR, and UPR groups respectively). However, the difference on the total score can mostly be attributed to the statement "I tried to Figure out how much longer I would have to keep my hand in the water" which was endorsed by eight subjects in the PR group and only three in the UPR group, suggesting that the difference was due to a differential amount of attention paid to the duration of the trials.

Next, correlations were run examining the relationship between coping behaviors during the task and the stress measures. In the NS and the UPR groups coping behaviors and

cardiovascular and self-report measures were not significantly correlated. However, in the PR group there was a negative correlation between distraction behaviors and SBP reactivity and mean pain and distress ratings (see Table 14). This suggests that only subjects who had information allowing them to predict the stressor duration showed effects of coping behavior on stress responding. Since these subjects engaged in fewer distraction behaviors than the UPR group this may partially explain why they had greater pain and distress reporting.

Immunological measures

The second hypothesis addressed the effects of the stressor on immune function and whether the predictability manipulation had a mediating effect on the immune changes. In order to answer both of these questions, repeated measures ANCOVA examined group differences in cell counts and lymphocyte proliferation to Con A and PWM.

Cell counts

Repeated measures ANCOVA examined changes in total number of leukocytes, percentages of lymphocytes, monocytes, and neutrophils over time using baseline values as covariates. There were no significant differences among the groups in any of the quantitative measures (see Tables 15 to 18).

Immune function

Lymphocyte proliferation to the two mitogens at two concentrations each were analyzed separately in repeated measures designs covarying for baseline levels. The manipulation significantly affected blastogenesis to Con A (10 ug/ml). ANCOVA yielded a group by time interaction, $F(4,60)=2.5$, $p<.05$. Only the unpredictable stressor group showed a significant

reduction in proliferation. The predictable stressor group showed no decline and values were comparable to those seen in the control group. Post-hoc analyses revealed a significant effect on proliferation after the second stressor period (Tukey, $p < .05$) (see Table 20, Figures 11 and 12). No significant effect was seen for the lower concentration of Con A (5ug/ml) (see Table 19). Lymphocyte proliferation to PWM was not significantly affected by the stressor or the predictability manipulation although the data reveal a similar pattern to that seen in response to Con A, with reductions in proliferation occurring in the UPR group (see Tables 21 and 22, Figures 13 and 14).

Correlations between stress measures and immunological outcomes were conducted to examine the possible contribution of indices of the stressfulness of the task to the decrease in proliferation to Con A (see Table 23). SBP change was negatively correlated with change scores in blastogenesis to Con A in the PR and the UPR groups indicating that high blood pressure reactivity was associated with decreases in proliferation. In addition DBP was negatively correlated with blastogenesis change in the UPR group. While pain ratings were not significantly correlated in the UPR group, distress showed some marginally significant negative correlations with blastogenesis. In the PR group pain and distress were negatively correlated with blastogenesis 20 minutes post stress.

The contribution of 'coping styles' to changes in proliferation to Con A was also examined (see Table 24). The amount of monitoring or distracting behaviors subjects used were not significantly associated with Con A mitogenesis in the UPR group but showed significant correlations in the PR group suggesting that distraction behaviors were associated with higher levels of blastogenesis in that group.

Although, changes in PWM induced blastogenesis in response to the stressor were not significant, the contribution of cardiovascular and psychological responses to these changes is still

of interest (see Table 25). In the PR group, self-report and BP reactivity were negatively correlated with proliferation to PWM (.01 ug/ml) 20 minutes post-stressor, suggesting that high stress was associated with low proliferation. In the UPR group, most significant correlations were found earlier during the session. Self-report and BP measures were associated with PWM blastogenesis immediately after the first task period. Distraction was only significantly correlated with PWM (.1 ug/ml) in the UPR group, suggesting that the use of distraction behavior was associated with higher proliferation (see Table 26).

In sum, there were no significant effects for the quantitative immune measures. For the functional measures, lymphocyte proliferation to Con A was significantly lowered by the unpredictable stressor and subjective and cardiovascular measures of stress were significantly correlated with the proliferative ability of the lymphocytes.

Discussion

Two sets of hypotheses were tested in this study. First, the effectiveness of a standard laboratory stressor, the cold pressor test, in increasing HR and BP and self-reported pain and distress and decreasing frustration tolerance on an unsolvable Feather task was examined. Further, the effects of predictability on these stress-induced changes were tested. While the first hypothesis was largely a replication of previous research with the goal of clarifying discrepancies in the current literature, the second hypothesis addressed a different issue. The study was designed to examine whether a cold pressor task could affect immunity and how these stress-related immune changes would be influenced by a psychological mediator, predictability.

Effects on stress responding

It was expected that the unpredictable task would be more stressful and that this would be reflected in all measures of stress including self-report, cardiovascular, and behavioral measures. While it was evident that the cold stressor was effective in raising BP and HR as well as pain and distress ratings, the mediating effect of predictability was less clear. Contrary to expectations, ratings of pain and distress were significantly higher in the PR group than either of the other groups. In addition, overall distress was higher in the PR group and was unaffected by the unpredictable stressor. The mood questionnaire showed no significant effects for the stressor except for a small overall difference on one of the subscales which was not confirmed by Tukey post-hoc analyses. This lack of an effect was probably due to the fact that this mood questionnaire had been designed to measure effects of different types of stressors in previous studies. It was not designed to pick up symptoms related to pain and cold and may therefore have been less sensitive to this particular stressor.

The cardiovascular changes that were observed in this study only partially supported the hypotheses. While the unpredictable stressor resulted in the expected increase in SBP, DBP was similarily affected by the unpredictable and the predictable stressors. Further, HR increased during the first part of the predictable stressor manipulation, but was unaffected by the unpredictable stressor. Cardiovascular changes were only detected during the first ten-minute stressor period suggesting that in both stressor groups subjects habituated relatively quickly.

The Feather task was used in order to pick up behavioral aftereffects of the stressors. Persistence on the unsolvable Figure was not affected by the stressor or the predictability manipulation. This may have been due to the delay in administering the task after the stressor; 25 to 30 minutes passed post-stressor before the Feather task could be completed because it was necessary to avoid affecting the immune measures taken 20 minutes post-stress. In most studies this task is administered within a very short period of time after stressor termination (Glass & Singer, 1972). The lack of effects on the Feather task could be explained by the fact that stress aftereffects may not persist for more than a few minutes after termination of the stressor and, therefore, may have disappeared during the 25 to 30-minute delay between stressor and Feather task administration.

The design used in this study was different from the methodology seen in the previous literature and so was the aspect of the manipulation that was rendered predictable or unpredictable. Most laboratory studies have varied information about the onset of a particular stimulus, whereas in this study it was information about the duration of the event once it had already started that was manipulated. The aspect of a stressor to which the information pertains could make a difference in terms of how this information affects the stressfulness of the event. This has been shown in studies conducted in hospital settings that have suggested that procedural information about an aversive medical procedure is not as helpful as sensory information about

the consequences of the procedure. The fact that this study used a different kind of information than has previous research may account for some of the unexpected findings. However, as has been pointed out in the review of the literature, the effects of predictability in the laboratory are not as clear as one might expect and many findings in previous research may help explain some of the results of the present study. While the majority of laboratory studies report an attenuation of stress responding when the event is made predictable some studies find no difference or the opposite effect.

The finding that subjects who were exposed to the predictable cold stressor reported more pain and distress receives little support in the literature because most studies have found the opposite to be true. Although, a few studies have reported no difference in aversiveness between predictable and unpredictable stimuli (Glass & Singer, 1972; Lykken et al., 1972), only one study could be found where subjects who received signaled shock reported greater symptoms of distress. However, this was confounded by a self-selection bias because subjects chose to be in the predictable condition (Miller et al., 1979). The preference studies have shown that a certain percentage of subjects when given a choice tend to choose the unpredictable stimulus suggesting that predictability is not always desirable to all individuals in all situations. It should be noted however that in the present study, there were no significant differences among the groups in terms of their preference ratings of predictability versus unpredictability.

In this study one could hypothesize that information can be either reassuring or threatening depending on what it is predicting. For example, knowing one is about to undergo a long cold pressor trial may be more stressful than not knowing and potentially hoping for the best. Conversely, knowing that the trial will be short, may be reassuring and cause less distress because one has the knowledge that it is endurable. In this case not having the information may be more stressful because the uncertainty about whether or not the pain will be bearable still

exists. In short, according to this argument, long trials should have been relatively more stressful in the PR group and short trials should have been more stressful in the UPR group. The difference in stressfulness of the different length trials cannot be determined in this study because subjective responses were only measured after four of the trials and the periodic cardiovascular readings were not able to capture responses to each individual trial since no continuous measures were taken. However, considering that more of the trials were of long duration in this study (i.e. 60% lasted 50 seconds or longer) could have biased the data towards showing a greater subjective distress effect in the PR group that should have been more distressed than the UPR group 60% of the time.

Another explanation for these results may be found in research conducted by Matthews and her colleagues. Matthews et al. (1980) postulated that the subjective aversiveness of a stimulus may be partly determined by the amount of attention that is paid to the stimulus. The more attention is focused on that stimulus the more aversive it will be perceived. This was also confirmed by Klemp and Rodin (1976) who found that subjects reported greater distress when they were told to attend to their emotional reactions to the shock. While the Matthews et al. study suggested that subjects tended to be more attentive to the stimulus when it was unpredictable, the reverse case scenerio could easily be possible. In the present study attention was drawn to the stimulus by giving subjects a countdown from the beginning to the end of each trial which made distraction away from the cold stressor rather difficult. In the UPR group, on the other hand, subjects listened to random numbers on the tape which had nothing to do with the stimulus itself. Here, instead of being constantly reminded of the painful stimulus through feedback about its duration, subjects in the UPR group could have actually used the random numbers as a distraction from the sensations they were experiencing. In addition, listening to meaningless random numbers may have allowed subjects to get distracted more easily and think

about other things rather than the aversive stimulus. Although, no direct measure of attention paid to the stimulus or to the subject's own emotional reactions were collected, the items asking about coping responses to the stressor tapped into the amount of distraction subjects used versus how much they focused on aspects of the task. Subjects in the UPR group had a somewhat lower monitoring score than PR subjects, i.e. they engaged in more distraction behaviors than PR subjects. In addition, there was an inverse relationship between the amount of distraction subjects used and their pain and distress ratings, indicating that distraction may have partially buffered the perceived aversiveness of the task. However, it should be noted that this questionnaire has not been validated prior to use in this study and that the data can be used for exploratory purposes at best. In addition, the differences between the groups on coping behaviors are mostly due to the PR subjects being more aware of the duration of the cold pressor trials rather than of the stimulus itself or of the sensations they were experiencing. Therefore, these results are not completely compatible with those seen in the studies by Matthews et al. and Klemp and Rodin.

It should also be noted that several studies that have examined the effects of attention on pain and distress have failed to find any stress buffering effects of distraction. A series of four studies especially pertinent to these findings was conducted by McCaul, Monsen, and Maki (1992) who reported that distraction did not buffer the stressful effects of a cold pressor task in the laboratory. However, this and other studies have manipulated distraction by using a task that could be stressful in itself since level of distraction is usually operationalized by using increasingly difficult and potentially stressful distraction tasks. This was not the case in the present study, since the hypothetical heightened level of distraction was due to listening to random numbers rather than having to complete a difficult task. The effects of attention on pain and distress reporting remains an attractive alternative explanation and should be further explored in future studies using better measures of attention.

The data for SBP showed the expected effects; SBP responses were significantly affected only by the unpredictable stressor. The cold pressor task has often been classified as a passive type of stressor, where a greater influence is thought to be exerted through alpha adrenergic receptors. The predominant vascular activity in response to this type of stressor generally induces a greater effect on DBP responsivity and less of a change in SBP and HR (Schneiderman & McCabe, 1989). One would therefore expect that subjects exposed to the cold pressor task would not show a significant increase in SBP, which is reflected in the responses seen in the PR group. The fact that the UPR group showed significant increases in SBP suggests that the unpredictability of the situation may have presented an additional stressor to these subjects that may be reflected in the magnitude of their SBP responses. Although the influence of unpredictability was not reflected in the subjects' self-reports of distress, the relatively high correlations between distress ratings and SBP reactivity suggest that SBP increases may have been partly due to heightened experiences of stress.

The data for the remaining cardiovascular measures did not support the hypothesis. Though DBP was responsive to the stressor itself, it was not significantly affected by the predictability manipulation despite the fact that a trend in the expected direction did exist during the second task period. There are very few laboratory studies of predictability that have used BP as a dependent variable, making this finding difficult to explain based on previous research. The studies that did assess BP, such as those by Carter and Beh (1989) and Zeichner et al. (1990) found this measure to be relatively insensitive to their particular predictability manipulations. One explanation for the lack of a predictability effect on DBP in this study may be that the cold pressor task is thought to be mostly a vascular type of stressor, affecting DBP to a greater extent than SBP or HR. The vascular effects of the cold stressor may have been strong enough to mask additional effects of the predictability manipulation, creating a 'ceiling effect' that did not leave

room for greater increases due to the psychological variable. This is especially pertinent to the first part of the stressor where the magnitude of the DBP responses is rather large. When DBP reactivity declined during the second phase of the task, probably as a result of habituation to the stressor, a predictability effect appeared to emerge, suggesting slower habituation in the UPR group, but was not large enough to reach statistical significance.

Finally, HR responsivity showed a pattern opposite to initial expectations. While the unpredictable cold pressor task elicited no change in HR levels from baseline, the predictable stressor significantly increased HR responses. As has been mentioned earlier, the cold pressor task is thought to be a more vascular type of stressor in which case a lack of HR response in one of the cold pressor groups is not surprising. In fact, the HR responses in the PR group, though statistically significant, were relatively small which is not unusual for this type of task. However, it has been suggested that the cold pressor task is also very sensitive to the experimental context in which it is presented (Schneiderman & McCabe, 1989). Research has suggested, for example, that the instructions surrounding this task are crucial in determining the cardiovascular reactions to it. When the instructions are highly challenging the cold pressor task can elicit significant increases in HR when compared to the same task administered with less challenging instructions (Dembroski, MacDougall, Herd, & Shields, 1979). It could be argued that the predictability manipulation presented a challenge to the subjects in that they received just enough information to feel like they would be able to prepare for the stressor. The finding that the PR group engaged in more monitoring types of behaviors than the UPR group tentatively supports this hypothesis since it would appear that active challenge would be associated with attentive behaviors and attitudes, whereas a stressor where no challenge is involved would be endured using distraction. Again, those data need to be interpreted with caution due to lack of psychometric information on this questionnaire and the fact that attention was not measured.

The discrepancy between SBP and HR is difficult to explain since both measures are usually thought to be affected in the same way. However, it is possible that the large increase in SBP in the UPR group may have caused a reflex bradycardia due to baroreceptor activation which may have prevented a HR increase in response to the unpredictable stressor. It should be noted, however, that this did not hold true for the PR group who also showed BP increases although SBP reactivity was not as large in that group. The study by Dembroski and colleagues (1979) probably offers the best support since their data showed that HR seemed more sensitive to challenging instructions in conjunction with the cold pressor test than did SBP, which may be more likely to accompany psychological distress associated with frustration, as is shown by the high correlations between pain and distress ratings and BP reactivity. It should also be noted that BP and HR were only measured intermittently throughout the session. Previous research has shown that HR may respond differently at different points of the stressor manipulation, for example differences between predictable and unpredictable stressors have been found depending on whether one measures HR during the anticipatory phase or the stressor phase (e.g., Monat et al., 1972). Since this study used an ambulatory monitor for both HR and BP measurements which could only take readings every two minutes at most, it was not possible to distinguish effectively between anticipatory and stressor responding. It is possible that crucial measurement periods were missed in this study and that continuous measurement of cardiovascular responses would have yielded more consistent results.

In addition, there appears to be a discrepancy between psychological stress reports and the cardiovascular measures. Although, correlations of stress and pain ratings with BP responsiveness were rather high in the PR group, very few significant correlations emerged in the UPR group. The same was true for correlations among the cardiovascular measures (SBP, DBP, and HR) and within measures across time. That is, in the UPR group cardiovascular

measures were not as highly correlated as in the PR group and some of the measures, especially SBP, appeared less stable over time. This latter effect was especially prominent when the ten individual SBP readings taken during the stressor were correlated suggesting large fluctuations over time in response to the unpredictable stressor. The predictable stressor on the other hand appeared to be associated with more stable SBP responding showing consistent positive correlations among the timepoints. Stress is thought to be an adaptive process where all systems work together for the purpose of meeting the demands of the stressor, i.e. to either fight or flee. This adaptive process is more effective the more information an individual has about crucial aspects of the stressor. It has been suggested by Lazarus and Folkman (1984) that when little is known about a stressor, the adaptive resources cannot be mobilized in a focused goal-directed manner, but rather they are more diffuse and general. Predictability of a stressor may therefore serve a role of energy conservation by allowing preparation in an organized fashion directed towards a well-defined goal. The fact that stress responses in the UPR group were not correlated as highly as one would expect suggests that a lack of information about an important part of the stressor may induce a breakdown of the adaptive process. That is, the responses that usually allow adaptation, including psychological and physiological responses, may diverge and fail to work together to effectively meet the demands posed by the threat when insufficient information is available.

In addition it has been hypothesized by Grings (1960) that heightened anticipatory arousal in a predictable situation may be the price to pay for a lessened impact of a given stressor (preparatory set hypothesis). Extending this hypothesis to the present study and combining it with the argument made above one may hypothesize that a steady level of arousal as seen in predictable situations may be more adaptive. That is, a steady though heightened level of arousal may lessen the impact of a stressor or its consequences when compared to large fluctuations in

arousal across time as it may occur in uncertain situations. The uncertainty about the duration of the stressor may have elicited fluctuations in moods as individuals were vacillating between hope and fear that might be reflected in a physiological instability characterized by fluctuations in these measures over time. Further, it may be the case that these fluctuations may produce greater wear and tear on the organism in the long run and have greater negative health consequences because they make habituation more difficult.

If this hypothesis, that unpredictable stressors lead to less efficient adaptation held true, then unpredictability should have negative consequences that in the predictable situation are attenuated due to better adaptation. The immunological data support this idea to the extent that a reduction in immune function can be thought of as an adverse consequence of stress that may hypothetically lead to negative health outcomes.

Immunological effects

The second set of hypotheses was concerned with the effects of the stressor and the predictability manipulation on immunity. It was hypothesized that the stressor would cause a reduction in mitogenesis and that predictability would buffer that effect.

The quantitative immune measures were unaffected by the stressor manipulation. This is consistent with previous laboratory studies that have used these measures (e.g. Zakowski et al., 1992). Only when subsets of lymphocytes such as T and B cells are measured using flow cytometry do differences between stress and control conditions appear, but even then they do not seem consistently replicable (e.g. Bachen et al., 1992). It appears that percentages of lymphocytes, monocytes, and neutrophils stay relatively stable in response to an acute stressor, but small changes in cell subsets, such as T-helper/T-suppressor cell ratios sometimes occur.

As far as lymphocyte proliferation to mitogens is concerned, the hypothesis was only

partly confirmed. While proliferation to PWM was not significantly affected by the manipulations, Con A stimulated blastogenesis was reduced in the UPR group. It appears that stressor predictability completely buffered the stressor's immunosuppressive effects. This is consistent with the study conducted by Mormede and colleagues (1989) reporting reductions in lymphocyte proliferation in response to an unpredictable stressor but no change to a predictable stressor in animals. Animal studies using control as the mediating variable have found similar effects. For example, Laudenslager and his co-workers reported that when lymphocyte proliferation was assessed following escapable and inescapable shock, only the inescapable shock produced a significant reduction in that measure (Laudenslager, Ryan, Drugan, Hyson, & Maier, 1983). This suggests that some stressors may only cause immune reductions if they are made uncontrollable or unpredictable implying that the psychological mediator is of great importance in determining outcomes at the immunological level. The decrease in lymphocyte proliferation in this study was significantly correlated with BP increases in the UPR group, reflecting sympathetic nervous system (SNS) arousal. Immune tissues have been found to be directly innervated by sympathetic neurons and in addition, lymphocytes bear adrenergic receptors (Bourne et al., 1974). This, in addition to the strong correlation between BP and blastogenesis changes indicates that SNS activity during the stressor may partly account for the immune change.

The fact that only some of the cardiovascular measures were associated with immune function in this study and self-report measures were only marginally correlated with blastogenesis results shows that SNS activity cannot fully explain the reductions in Con A mitogenesis. In addition, it appears that the predictable stressor was more stressful than the unpredictable one when self-reported pain and distress are considered. It is, therefore, difficult to explain the reductions in lymphocyte proliferation solely in terms of sympathetic nervous system activation.

Stress affects a variety of neuroendocrines many of which are known to directly act on immune cells through receptors. For example, endogenous opioid peptides (EOP) have been implicated in the effects of uncontrollable stressors on the immune system. Lymphocytes are known to have opiate receptors (Mehrishi & Mills, 1983) and beta-endorphins can suppress lymphocyte proliferation in vitro (McCain, Lamister, Bozzone, & Grbic, 1982). It is thought that painful stimulation does not always induce EOP release. Laudenslager et al. (1983) reported that inescapable shock which induced an opioid type analgesia, i.e. analgesia that was reversible by naloxone, was associated with decreases in lymphocyte proliferation in animals. However, no immune effect was seen in response to escapable shock which was not associated with increased opioid levels. These reductions in blastogenesis were attributed to increases in EOPs which acted on the opiate receptors on lymphocytes to reduce their functioning.

It could be hypothesized here that the unpredictable pain stimulus in the present study may be comparable to the uncontrollable shock in the animal studies. That is, the unpredictable cold stressor may have induced a greater release of EOPs than the predictable stressor. Since EOPs are known to affect lymphocytes, a large rise in EOP levels may lead to a reduction in these cells' proliferative ability. Therefore, EOP release in response to the unpredictable stressor could account for the reduction in proliferation that was not seen after the predictable stressor. In addition, the unpredictable stressor was associated with lower pain reporting. While at first glance this seems to be counterintuitive, i.e. low pain ratings should be associated with less distress and therefore with a lower impact on the immune system, the hypothesized opioid release would provide an explanation. Endogenous opioids are known to increase pain threshold and if the unpredictable stressor actually was associated with a greater increase in EOPs one would expect attenuated pain responses to that stressor. The putative release of EOP in response to the unpredictable pain stimulus could explain the lower pain ratings in comparison to the ratings seen

in the predictable stressor group. Finally, the unpredictable stressor was associated with very little HR reactivity. Again, if SNS activation were responsible for the effects one would expect high HR to be associated with lower immune function. However, the opposite appears to be the case, i.e. the group with the lowest HR responsiveness also had the greatest reduction in proliferation. Data on the effects of EOPs on vagal tone may suggest a potential mechanism for these findings. In animals EOPs have been shown to reduce HR through vagal influence (Wei & Kiang, 1984). A hypothetical release of EOPs during the unpredictable stressor could therefore explain the lack of HR reactivity. If increased levels of EOPs during the unpredictable stressor reduced HR this effect may have overridden the usual stress-related sympathetic effect on HR reactivity resulting in a lack of increased cardiac activity in this group.

Using this comparison between uncontrollable stressors from animal research and the unpredictable stressor from this study by suggesting a hypothetical common mediator, EOP release, one can start to explain some of the findings that at first glance seemed contradictory. If the unpredictable stressor actually did lead to a greater increase in EOPs the attenuated pain responses and the lack of HR reactivity in conjunction with the reduction in lymphocyte proliferation can easily be explained. However, since no measures of neuropeptides were included in this study no conclusions on the mechanisms for the immune, cardiovascular, and pain responses can be drawn from these data. At this point one can merely speculate on the potential mediators.

It should also be noted that there are several limitations to the opioid hypothesis. The effects of EOP's on immune function are still controversial with some studies finding higher levels to be associated with increased immune function (e.g. Darko, Irwin, Risch, & Gillin, 1992). Further, the meaning of non-opioid analgesia has yet to be determined. It is unclear which neuroendocrines may be involved in that process and why non-opioid analgesia is not

associated with immunological changes.

Another point that requires further explanation is that the reduction in proliferation was only seen in response to Con A (10 ug/ml) but not to PWM. Although PWM stimulated proliferation was reduced in the UPR group, this trend did not reach statistical significance. The two mitogens are fundamentally different in that they are thought to stimulate different types of lymphocytes. Con A predominantly affects T-lymphocytes, whereas PWM predominantly stimulates B-cells (Stites, 1987). It is possible that T-cell functioning is more susceptible to certain types of stressors and psychological manipulations potentially by virtue of the endocrine receptors they bear and how they are affected by different neuroendocrines whose release depends on the type of stressor used. In a similar study recently conducted in this laboratory, it was found that Con A induced proliferation was reduced to a greater extent and more rapidly than PWM blastogenesis (Zakowski, Cohen, Hall, Wollman, & Baum, unpublished manuscript). To the extend that PWM predominantly affects B cells it could be hypothesized that since B-cells are late to respond in the presence of an antigen compared to T-cells, the same pattern may be followed when lymphocytes are affected by stress hormones, i.e. B-cells may be activated later in the chain of events. It is possible that their adrenergic receptors are not as sensitive to catecholamines or have a different threshold than the T-cell receptors. In addition, it has been suggested that T-suppressor cells, which are the primary cells activated by Con A stimulation, have a greater density of adrenergic binding sites than other lymphocytes (Kahn, Sansoni, Silverman, Engleman, & Melmon, 1986). This may offer another explanation for the greater reduction in Con A blastogenesis, i.e. if CD8 cells have more adrenergic receptors, more hormones can bind which in turn may accelerate the effects on the cells function and at the same time reduce the availability of catecholamines to bind to receptors on other types of lymphocytes. However, it should be noted that there is no evidence for differential sensitivity of adrenergic

receptors on different types of lymphocytes and the hypothesis that B-cells may show delayed responding to stress hormones has not been shown. The hypotheses for the different findings observed for Con A and PWM induced proliferation are purely speculative at this point. To date, very little is known about how different stressors affect different neuroendocrines and by which mechanisms stress and psychological factors affect different types of immune cells. In fact, previous research has been faced with similar problems of discrepancies among different immune measures. However, in this study, PWM and Con A stimulated proliferation showed similar patterns of responding to the manipulation, i.e. both were reduced in response to the unpredictable stressor, and were both correlated with self-report and BP reactivity.

Finally, proliferation to Con A was only significantly affected at one of two doses of the mitogen (10 ug/ml). Since the optimal dose of a mitogen to obtain maximal stimulation is thought to vary among individuals the fact that one only one of the concentrations showed an effect is not unusual. A previous study conducted in the same laboratory also found stress effects with Con A at 10 ug/ml but not 5 ug/ml (Zakowski et al., unpublished manuscript). This suggests that this dose may be the optimal one to use in this laboratory and with the population chosen for these studies. More detailed studies need to be conducted assessing different neuroendocrines and a wider range of immune parameters in order to attempt to explain which immune cells and tissues are affected by which stressors and which assays may be the most sensitive ones to use.

Summary

In summary, the hypotheses were partly confirmed. It was initially expected that the unpredictable stressor would be more stressful and entail the greatest immune reduction. While some of the results of this study supported these ideas others require further explanation. It was shown in this research that subjects reported the predictable stressor to be more painful and stressful. This was mirrored by their HR responses, which were increased during the first task phase, but not by their SBP or DBP responses. Lymphocyte proliferation to Con A was reduced by the unpredictable stressor only.

While many explanations are possible, there are three hypotheses that seem to be the most attractive. First, the discrepancy between self-report and physiological measures can be explained by a differential amount of attention paid to the aversive stimuli. That is, it was proposed that subjects in the predictable stressor group were forced to pay greater attention to the stressor and the pain associated with it because the countdown on the tape kept them from distracting themselves. To the extend that distraction helps reduce distress in some instances attention may be able to account for the increased pain and distress ratings in the predictable stressor group.

In light of the differences seen among the measures of stress and within measures across time, it was suggested that unpredictability or lack of information about a crucial aspect of the stressor may impair adaptive coping and mobilization of resources that act together to enable the organism to fight or flee. In that case, it was suggested that if the divergence of different stress responses is actually maladaptive, adverse consequences of unpredictability should be seen either in the form of behavioral aftereffects or health consequences. The behavioral measure used in this study, i.e. the Feather task, was not affected probably as a result of poor timing of administration. While health consequences cannot be measured in response to such a short term

stressor, immunity, which is generally associated with health, was reduced as a result of the unpredictable situation. To the extent that a reduction in immune function can be considered an adverse consequence of stress, it can be concluded that the decrease in lymphocyte proliferation might confirm the idea that unpredictability may lead to poor adaptation and negative consequences.

Another explanation that has been offered and appears to fit with several of the findings is the opioid hypothesis. If unpredictability is similar to uncontrollability in conjunction with a pain stressor, one can speculate that comparable patterns of neuropeptide release may hold true. It was suggested that unpredictable pain could result in a greater opioid release than predictable pain. This could account for the lower pain perception and lack of HR reactivity in the unpredictable group while still supporting a reduction in lymphocyte responsiveness to mitogens through action on opiate receptors on these immune cells.

While these findings require replication, they do raise important questions about the adaptive effects of predictability of a stressor. Depending on the endpoints being studied, one may come to different conclusions on the beneficial effects of providing individuals with information about aspects of a stressful event. While the subjective responses to the stressor may point in the direction of omitting information in order to give subjects the opportunity to distract themselves in the face of an uncontrollable aversive stimulus, when physiological and immune responses are considered, a different picture emerges. The question then is, if subjective and physiological responses are not always related, which endpoints should be used in order to judge on the potential benefits of enhancing information about aspects of a stressful event.

These data underscore the importance of taking multiple measures of stress. No laboratory studies that have examined the effects of predictability, to date, have incorporated self-report, behavioral, cardiovascular, and immune assessments simultaneously. It is therefore not

surprising that discrepancies among these measures have not been picked up in prior research. Future research should be done measuring stress at multiple levels in order to clarify the issue of which type of information is useful in attenuating distress and in order to establish mechanisms by which predictability may protect against potential adverse health consequences of stress. It would be especially useful to include assessments of hormones and neuropeptides in studies of predictability so that some of the hypotheses suggested above can be examined.

In order to test hypotheses that have been made in an attempt to explain some of the discrepant findings concerning self-report, cardiovascular, and immune measures the following improvements or expansions on the present design would be useful. First, in order to assess why the predictable stressor elicited greater pain and stress reporting a questionnaire assessing the amount of attention paid to the stressor or the pain sensations would be useful. In addition, one could try to equate attention in the two groups through appropriate instructions (see Matthews et al., 1980) or use of distraction techniques. Further, in order to assess whether predictability is beneficial only when the information is reassuring but less so when it is threatening, self-report should be assessed during stressor trials that vary in their degree of aversiveness. That is, in the present study, pain and distress ratings should have been obtained after the short and the long cold pressor trials and this could have been supplemented by preference ratings to assess whether subjects preferred predictability during all trials regardless of their length or aversivenss.

It was also suggested that the discrepancy between self-report and BP responding may have been due to the infrequent and intermittent cardiovascular measurements. In order to be able to assess what is occurring at the cardiovascular level continuous measurement techniques would provide a great improvement to this design. This in conjunction with frequent blood sampling for endocrine assessments would increase our knowledge about subjects' responses at the different phases of the stressor, i.e. anticipation, impact, and recovery. Better measurement

techniques would also allow us to address the question whether unpredictable stressors are associated with greater fluctuations in stress responses than predictable ones and which response patterns may have the most adverse consequences.

Table 1: Human acute stress and immunity studies.

	Manuck et al., 1991	Bachen et al., 1992	Zakowski et al., 1992	Naliboff et al., 1992	Weisse et al. 1990	Sieber et al., 1992
Subjects (age)	25 men (18-30)	44 men (19-25)	29 men (18-45)	23 women (21-41,>65)	22 men (21-36)	64 men (18-26)
Fasting	?	12 hours	n/a	8 hours	morning	n/a
Stressor	computer Stroop/ MA	computer Stroop	film recall	MA	noise shock	noise
Task Duration	20 min	21 min	30 min	12 min.	30 min.	2 x 20 min.
Immune measures	WBA: PHA prolif.	WBA: PHA, cell counts	Sep.: Con A, PHA	Sep.: NK	Sep.: Con A, PHA	Sep.: NK
Stress measures	BP, HR, Epi, NE, cortisol	BP, HR	BP, HR, cortisol, self-rep.	BP/HR, SC, Epi, NE, DA, self-rep.	self-rep.	behavior
Baseline immune (min. post-iv)	28 min.	30 min.	0 min.	30 min.	0 min.	0 min.
Post-stress immune (min. since onset)	20 min	21 min.	15 min 60 min 90 min 120 min	12 min.	30 min 50 min 150 min	20 min. 70 min. 24 hrs. 72 hrs.
Stress Group	no change	small decrease	decrease	inc. in young		
High reactors /no ctrl	decrease in PHA	n/a	decrease increase to recall	n/a	no change	decrease in NK
Low reactors /ctrl	no change	n/a	no change	n/a	decrease in ConA	no change
Control group	no change	increase	increase	no change		no change
Problems					manip. check	manip. check

WBA: Whole blood lymphocyte assay. Sep.: Separated lymphocyte assay.
Ctrl.: Experimental groups that received the perceived control manipulation.

Table 2: Ratings on predictability questionnaire (SD) by experimental groups. Scales range from 0 = not at all to 7 = extremely

	NS	PR	UPR
1. During each trial were you able to predict when the trial would end?	4.9 (2.1)	3.8 (2.4)	0.9(1.1)
2. After each one of the trials, were you able to predict approximately how long the following trial would last?	0.3 (0.6)	1.3 (1.6)	1.2 (1.2)
3. Did the numbers on the tape help you judge how long each trial would last?	4.6 (2.3)	4.8 (2.2)	0.7 (1.5)
4. If you had to do this task again would you want to be told at the beginning of each trial how many seconds you will have to keep your hand in the water?	2.7 (2.3)	4.1 (2.4)	2.0 (2.3)
5. How much control did you feel you had over what happened to you during the tasks?	3.5 (2.0)	2.6 (1.5)	1.8 (1.7)
6. How stressed did you feel during the tasks?	0.9 (1.2)	3.4 (1.7)	1.4 (1.0)

Table 3: Positive affect ratings (SD) on mood questionnaire at baseline and after the two task periods by experimental group. High ratings signify high positive affect.

	Baseline	**Task 1**	**Task 2**
NS	13.5 (3.6)	13.6 (4.1)	12.6 (4.1)
PR	12.5 (5.4)	8.2 (4.8)	7.5 (6.2)
UPR	11.5 (4.8)	8.7 (4.1)	9.3 (4.7)

Main effect for group: $F(2,30)=4.31$, $p<.02$
Group by task interaction: $F(2,31)=.63$, $p<.54$

Table 4: Negative affect ratings (SD) from mood questionnaire at baseline and after the two task periods by experimental groups. High ratings signify high negative affect.

	Baseline	**Task 1**	**Task 2**
NS	1.6 (2.0)	1.9 (3.5)	1.9 (3.9)
PR	5.1 (10.3)	4.7 (5.5)	3.3 (3.9)
UPR	2.2 (4.9)	5.7 (6.8)	2.9 (4.5)

Main effect for group: $F(2,27)=.71$, $p<.50$
Group by task interaction: $F(2,28)=1.25$, $p<.30$

Table 5: Energy ratings (SD) on mood questionnaire at baseline and after the two task periods by experimental groups. High ratings signify low energy.

	Baseline	**Task 1**	**Task 2**
NS	5.3 (3.9)	6.0 (4.0)	6.4 (4.1)
PR	6.5 (3.8)	6.6 (3.8)	6.4 (4.2)
UPR	5.9 (2.8)	6.5 (2.7)	6.7 (2.8)

Main effect for group: $F(2,29)=.2$, $p<.82$
Group by task interaction: $F(2,30)=.4$, $p<.67$

Table 6: Pain ratings (SD) after trials 2, 5, 7, and 9 by experimental group. High ratings signify high pain reporting.

	Trial 2	**Trial 5**	**Trial 7**	**Trial 9**
NS	0.3 (0.8)	0.2 (0.6)	0.2 (0.6)	0.1 (0.3)
PR	4.1 (0.8)	4.0 (1.4)	3.4 (1.6)	4.5 (1.4)
UPR	3.7 (1.2)	3.4 (1.0)	2.7 91.2)	3.0 (1.3)

Main effect for group: $F(2,32)=55.7$, $p<.0001$
Group by time interaction: $F(6,58)=5.6$, $p<.0001$

Table 7: Distress ratings (SD) after trials 2, 5, 7, and 9 by experimental group. High ratings signify high pain reporting.

	Trial 2	**Trial 5**	**Trial 7**	**Trial 9**
NS	0.3 (0.6)	0.3 (0.6)	0.2 (0.4)	0.2 (0.4)
PR	3.6 (0.8)	3.6 (1.2)	3.0 (1.5)	4.0 (1.7)
UPR	2.9 (1.8)	2.2 (1.5)	2.0 (1.4)	2.4 (1.6)

Main effect for group: $F(2,32)=27.7$, $p<.0001$
Group by time interaction: $F(6,58)=2.3$, $p<.045$

Table 8: Mean SBP (SD) in mm/Hg at baseline and during the two task periods by experimental group

	Baseline	**Task 1**	**Task 2**
NS	117.9 (10.8)	121.4 (10.5)	119.3 (10.4)
PR	115.0 (10.2)	125.4 (11.0)	120.3 (9.6)
UPR	122.1 (8.8)	137.3 (12.2)	128.4 (11.7)

Main effect for group: $F(2,31)=5.7$, $p<.008$
Group by task interaction: $F(2,32)=3.2$, $p<.05$

Table 9: Mean DBP (SD) in mm/Hg at baseline and during the two task periods by experimental group

	Baseline	**Task 1**	**Task 2**
NS	69.3 (8.7)	73.1 (7.1)	73.9 (7.1)
PR	65.5 (9.4)	77.8 (11.6)	70.3 (9.7)
UPR	70.7 (7.7)	83.5 (9.4)	79.5 (9.5)

Main effect for group: $F(2,31)=4.28$, $p<.02$
Group by task interaction: $F(2,32)=6.21$, $p<.005$

Table 10: Mean HR (SD) in bpm at baseline and during the two task periods by experimental group.

	Baseline	**Task 1**	**Task 2**
NS	67.9 (8.7)	66.4 (8.0)	67.3 (7.3)
PR	63.8 (7.3)	67.2 (8.7)	61.9 (8.7)
UPR	65.2 (7.7)	63.8 (8.9)	62.4 (7.1)

Main effect for group: $F(2,31)=1.2$, $p<.32$
Group by task interaction: $F(2,32)=7.0$, $p<.003$

Table 11: Correlation between mean self-reported pain and distress ratings and mean BP and HR change scores.

No Stress

	SBP change	DBP change	HR change
Pain	-.09	-.04	.17
Distress	.40 *	.23	.003

Predictable Stressor

	SBP change	DBP change	HR change
Pain	.86 ***	.87 ***	.24
Distress	.67 ***	.59 **	-.09

Unpredictable Stressor

	SBP change	DBP change	HR change
Pain	.36	.31	-.49 **
Distress	.69 ***	.39	-.24

* $p<.1$
** $p<.05$
*** $p<.01$ (one-tailed test)

Table 12: Correlations among cardiovascular changes during the first and the second task period (T1 and T2) by experimental group:

No Stress:

	T1: SBP	T1: DBP	T1: HR	T2: SBP	T2: DBP	T2: HR
T1: SBP		.36	.46 *	.86 ***	-.08	.11
T1: DBP			.15	.37	.55 **	.28
T1: HR				.22	-.29	.81 ***
T2: SBP					.20	-.06
T2: DBP						-.25
T2: HR						

Predictable Stressor:

	T1: SBP	T1: DBP	T1: HR	T2: SBP	T2: DBP	T2: HR
T1: SBP		.73 ***	.55 **	.67 **	.42 *	.32
T1: DBP			.54 **	.72 ***	.66 ***	.21
T1: HR				.29	.32	.63 **
T2: SBP					.71 ***	.28
T2: DBP						.11
T2: HR						

Unpredictable Stressor:

	T1: SBP	T1: DBP	T1: HR	T2: SBP	T2: DBP	T2: HR
T1: SBP		.53 **	-.29	.29	.23	-.32
T1: DBP			.18	.34	.81 ***	.01
T1: HR				.27	.55 **	.56 **
T2: SBP					.41 *	.08
T2: DBP						.40 *
T2: HR						

* $p<.1$ ** $p<.05$ *** $p<.01$ (one-tailed)

Table 13: Number of trials (SD) on the two figures of the Feather task by experimental group.

	Unsolvable figure	**Solvable figure**
NS	11.7 (6.8)	2.3 (2.1)
PR	18.5 (15.1)	2.6 (4.8)
UPR	16.8 (12.4)	2.0 (1.9)

Unsolvable figure: Main effect for group: $F(2, 34)=1.1$, $p<.36$
Solvable figure: Main effect for group: $F(2, 34)=.1$, $p<.89$

Table 14: Correlations between amount of distraction behavior used and mean pain and distress and mean BP and HR changes.

No Stress

	Pain	Distress	SBP	DBP	HR
Distraction	.47 *	-.19	-.38	-.32	-.02

Predictable Stressor

	Pain	Distress	SBP	DBP	HR
Distraction	-.51 **	-.56 **	-.63 ***	-.41 *	.17

Unpredictable Stressor

	Pain	Distress	SBP	DBP	HR
Distraction	-.13	.28	-.07	-.17	.21

* $p<.1$
** $p<.05$
*** $p<.01$ (one-tailed test)

Table 15: White blood counts per mm^3 (SD) at baseline and three task periods for the experimental groups.

	Baseline	**Task 1**	**Task 2**	**20 min**
NS	4.9 (1.3)	4.9 (1.6)	4.9 (1.5)	5.0 (1.4)
PR	7.0 (3.1)	6.8 (3.0)	6.9 (3.2)	6.7 (2.7)
UPR	5.6 (1.0)	5.9 (0.9)	5.7 (1.1)	5.6 (1.1)

Main effect for group: $F(2,29)=.55$, $p<.58$
Group by time interaction: $F(4,60)=1.53$, $p<.2$

Table 16: Percentage of neutrophils (SD) at baseline and three task periods for the experimental groups.

	Baseline	Task 1	Task 2	20 min
NS	53.2 (6.8)	53.9 (8.6)	57.6 (8.3)	57.9(10.3)
PR	58.4 (9.9)	56.2 (11.1)	57.7 (10.1)	63.5 (8.2)
UPR	49.8 (10.6)	46.8 (11.8)	51.4 (11.2)	53.7(13.9)

Main effect for group: $F(2,29)=.78$, $p<.47$
Group by time interaction: $F(4,60)=.72$, $p<.58$

Table 17: Percentages of lymphocytes (SD) at baseline and three task periods for the experimental groups.

	Baseline	Task 1	Task 2	20 min
NS	35.0 (6.6)	33.5 (6.9)	30.5 (7.5)	30.9(10.3)
PR	31.4 (9.5)	32.9 (9.4)	29.1 (9.6)	24.8 (7.1)
UPR	38.6 (9.8)	42.4 (11.2)	37.1 (12.9)	35.3(12.2)

Main effect for group: $F(2,29)=1.52$, $p<.23$
Group by time interaction: $F(4,60)=.73$, $p<.57$

Table 18: Percentages of monocytes (SD) at baseline and three task periods for the experimental groups.

	Baseline	Task 1	Task 2	20 min
NS	8.4 (4.0)	9.0 (4.0)	8.6 (3.2)	8.5 (4.1)
PR	6.9 (3.3)	9.5 (7.4)	10.0 (4.7)	8.5 (3.0)
UPR	6.7 (2.7)	7.5 (4.1)	7.6 (4.2)	7.3 (4.5)

Main effect for group: $F(2,29)=1.43$, $p<.25$
Group by time interaction: $F(4,60)=.14$, $p<.96$

Table 19: Lymphocyte proliferation to Con A (5 ug/ml) and SD in dpm at baseline and three task periods by experimental group.

	Baseline	**Task 1**	**Task 2**	**20 min**
NS	165450 (7802)	147432 (62155)	149868 (58363)	143597 (70487)
PR	137385 (61460)	134413 (66925)	137008 (67289)	129456 (72601)
UPR	186679 (83328)	181162 (72036)	166965 (78824)	166442 (66712)

Main effect for group: $F(2,31)=.88$, $p<.42$
Group by time interaction: $F(4,64)=1.04$, $p<.39$

Table 20: Lymphocyte proliferation to Con A (10 ug/ml) and SD in dpm at baseline and three task periods by experimental groups.

	Baseline	**Task 1**	**Task 2**	**20 min**
NS	187664 (84145)	178879 (69577)	193304 (74154)	177906 (73956)
PR	169583 (75947)	169471 (74457)	182429 (87789)	168483 (85092)
UPR	219097 (100068)	202049 (78544)	196935 (80539)	203584 (85555)

Main effect for group: $F(2,31)=1.41$, $p<.26$
Group by time interaction: $F(4,60)=2.49$, $p<.05$

Table 21: Lymphocyte proliferation to PWM (.01 ug/ml) and SD in dpm at baseline and three task periods by experimental groups.

	Baseline	**Task 1**	**Task 2**	**20 min**
NS	112745 (71783)	116101 (63748)	120770 (54058)	113052 (72474)
PR	91896 (58307)	104764 (71193)	105170 (63287)	95393 (65148)
UPR	127511 (83332)	120562 (81765)	127242 (79384)	120364 (67386)

Main effect for group: $F(2,30)=.53$, $p<.59$
Group by time interaction: $F(4,62)=.23$, $p<.92$

Table 22: Lymphocyte proliferation to PWM (.1 ug/ml) and SD in dpm at baseline and three task periods by experimental groups.

	Baseline	**Task 1**	**Task 2**	**20 min**
NS	118995 (66508)	119528 (63598)	120438 (59018)	115280 (70129)
PR	102868 (71588)	108592 (70345)	112237 (73641)	102375 (69630)
UPR	123904 (79844)	110843 (64388)	118325 (70519)	116701 (65404)

Main effect for group: $F(2,31)=1.27$, $p<.29$
Group by time interaction: $F(4,64)=.41$, $p<.80$

Table 23: Correlations of pain, distress, BP and HR change with Con A (5 and 10 ug/ml) blastogenesis change scores after the first five trials, the second five trials, and 20 minutes post-task.

No Stress

	Con A (5ug/ml)			Con A (10ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	.02	-.09	-.08	-.11	-.19	-.05
Distress	.03	.25	.03	.29	.54**	.31
SBP change	-.20	-.09	-.58**	-.05	.06	-.35
DBP change	-.04	-.10	-.28	-.29	-.05	-.22
HR change	.35	-.02	-.06	.16	-.06	.1

Predictable Stressor

	Con A (5 ug/ml)			Con A (10 ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	-.24	-.18	-.69***	.14	-.12	-.43*
Distress	-.32	-.14	-.66***	.32	-.23	-.49*
SBP change	-.10	-.22	-.48*	-.09	-.28	-.46*
DBP change	-.19	-.19	-.45*	-.06	.00	-.29
HR change	-.09	-.13	-.31	-.22	.02	-.25

Unpredictable Stressor

	Con A (5 ug/ml)			Con A (10 ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	-.02	-.10	-.31	-.13	-.05	-.1
Distress	-.52**	-.44*	-.43*	-.42*	-.47*	-.44*
SBP change	-.46*	-.32	-.38	-.25	-.31	-.50**
DBP change	-.65***	-.21	-.43*	-.68***	-.40*	-.61**
HR change	-.14	.45*	.36	-.28	.15	-.02

* $p<.1$ ** $p<.05$ *** $p<.01$ (one-tailed test)

Table 24: Correlations between amount of distraction used and Con A (5 and 10 ug/ml) blastogenesis change scores after the first five trials, the second five trials, and 20 minutes post-task.

No Stress

	Con A (5 ug/ml)			Con A (10 ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	-.25	-.67***	-.14	-.36	-.45*	-.15

Predictable Stressor

	Con A (5ug/ml)			Con A (10 ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	-.04	-.01	.07	.21	.53**	.59**

Unpredictable Stressor

	Con A (5ug/ml)			Con A (10 ug/ml)		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	-.12	-.26	.17	.02	-.03	.11

* $p<.1$
** $p<.05$
*** $p<.01$

Table 25: Correlations of pain, distress, BP, and HR changes with PWM (.01 and .1 ug/ml) blastogenesis change scores after the first five trials, the second five trials, and 20 minutes post-task.

No Stress

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	.12	.12	.14	-.22	-.05	-.03
Distress	-.19	.06	-.24	.01	.01	-.47*
SBP change	-.13	-.16	-.54**	-.005	-.09	-.33
DBP change	-.47*	-.3	-.37	-.36	-.30	-.34
HR change	-.13	-.19	-.31	-.28	-.44*	-.31

Predictable Stressor

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	-.47	.05	-.78***	-.08	-.40	-.46*
Distress	-.49*	-.05	-.66***	-.06	.38	-.13
SBP change	-.25	-.05	-.63**	.08	.35	-.22
DBP change	-.45*	-.04	-.82***	-.20	.27	-.62**
HR change	.05	.16	-.23	.15	.18	-.15

Unpredictable Stressor

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Pain	-.24	.16	-.06	-.13	.11	-.04
Distress	-.55**	.00	-.18	-.55**	.13	-.09
SBP change	-.74***	-.13	-.12	-.41*	.01	-.10
DBP change	-.41*	-.24	-.20	-.72***	-.28	-.25
HR change	.39*	.16	.40*	-.15	.26	.38

* p<.1 ** p<.05 *** p<.01 (one-tailed test)

Table 26: Correlations between amount of distraction used and PWM (.01 and .1 ug/ml) blastogenesis change scores after the first five trials, the second five trials, and 20 minutes post-task.

No Stress

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	-.08	-.35	.29	-.27	-.34	.37

Predictable Stressor

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	.18	.20	.45*	-.15	-.27	-.06

Unpredictable Stressor

	PWM .01 ug/ml			PWM .1 ug/ml		
	Task1	**Task2**	**20min**	**Task1**	**Task2**	**20min**
Distraction	.11	.14	.44*	.07	.49**	.52**

* $p<.1$
** $p<.01$ one-tailed test

Figure caption 1: Ratings of predictability of stressor duration in response to two separate questions: 1. "During each trial were you able to predict when it (the trial) would end?", 2. "Did the numbers on the tape help you judge how long each trial would last?". Mean ratings are shown for the no stress control group (NS), the predictable stressor group (PR) and the unpredictable stressor group (UPR). Tukey post-hoc analysis revealed signifcant differences between the UPR group compared to the NS and the PR groups.

Figure 1: Predictability Ratings

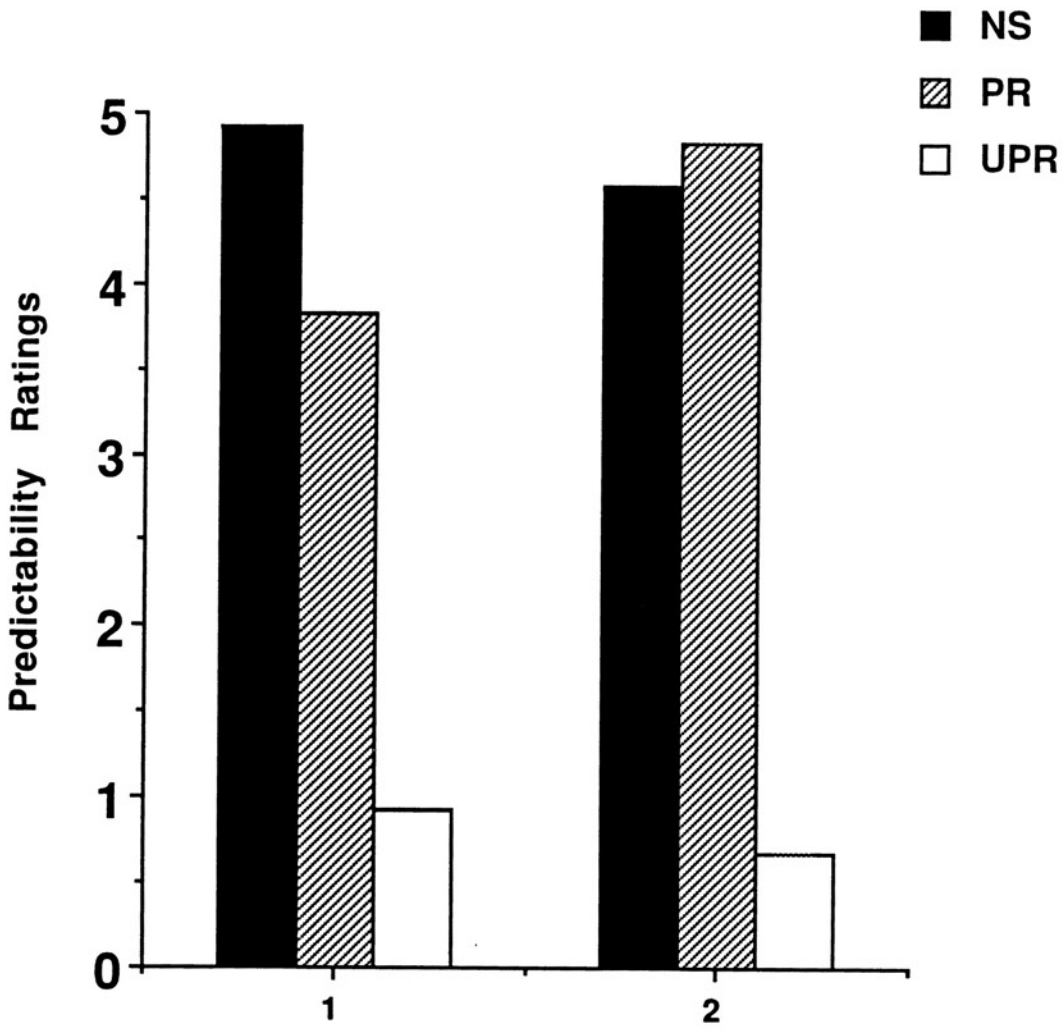


Figure caption 2: Rating of stressfulness of the tasks in response to a single question asked at the end of the second task period: "How stressed did you feel during the tasks?". Tukey post-hoc analysis showed that the UPR group had signficantly higher ratings than the NS or the PR group.

Figure 2: Overall Stress Rating (post-task)

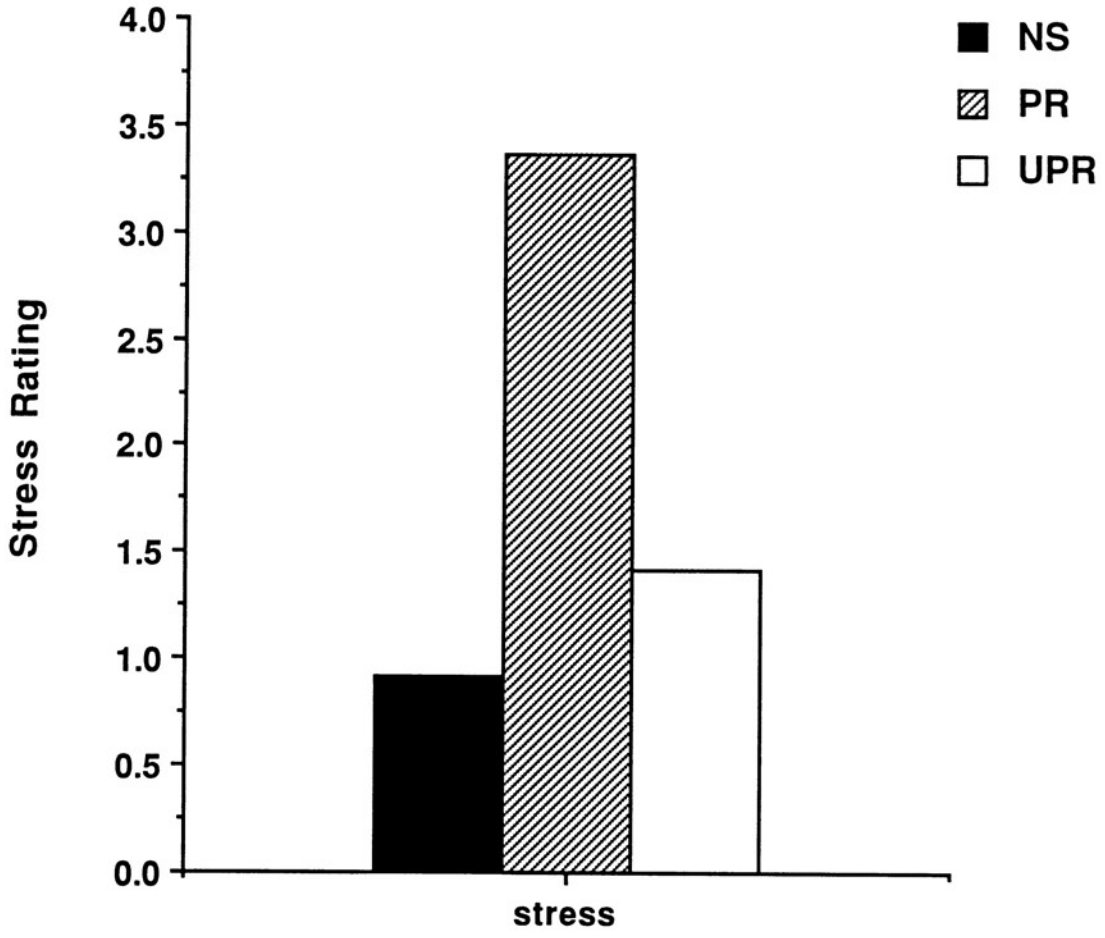


Figure caption 3: Pain ratings after the second, fourth, seventh, and ninth cold/warm pressor trials. Tukey post-hoc analysis revealed significant differences between the two stressor groups (PR and UPR) and the no stress controls (NS) for all trials. In addition, after the ninth trial the PR group gave significantly higher ratings than the UPR group.

Figure 3: Pain Ratings

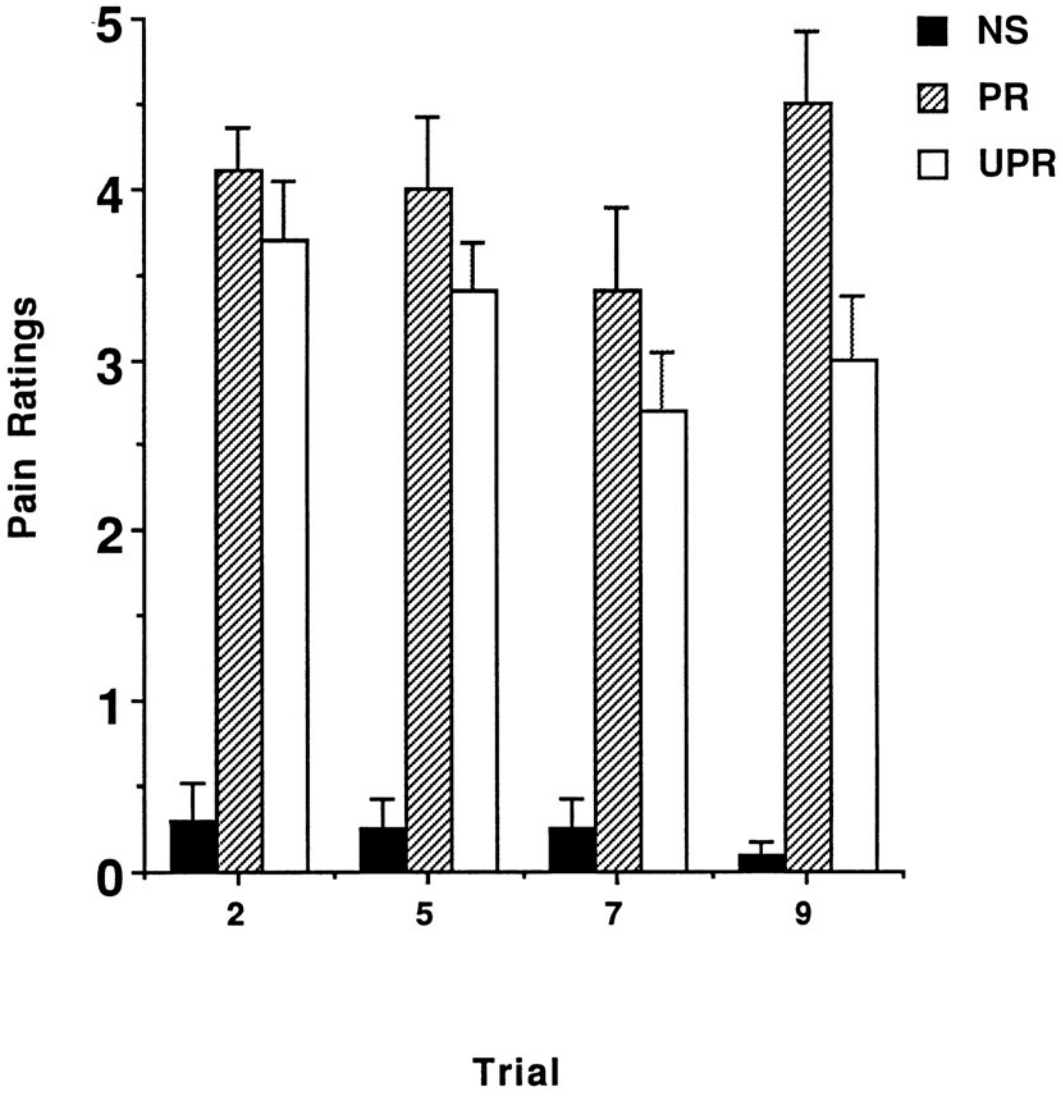


Figure caption 4: Distress ratings after the second, fourth, seventh, and ninth cold/warm pressor trials. Tukey post-hoc analysis revealed significant differences between the two stressor groups (PR and UPR) and the no stress controls (NS) for all trials. In addition, after the fifth and ninth trials the PR group gave significantly higher ratings than the UPR group.

Figure 4: Distress Ratings

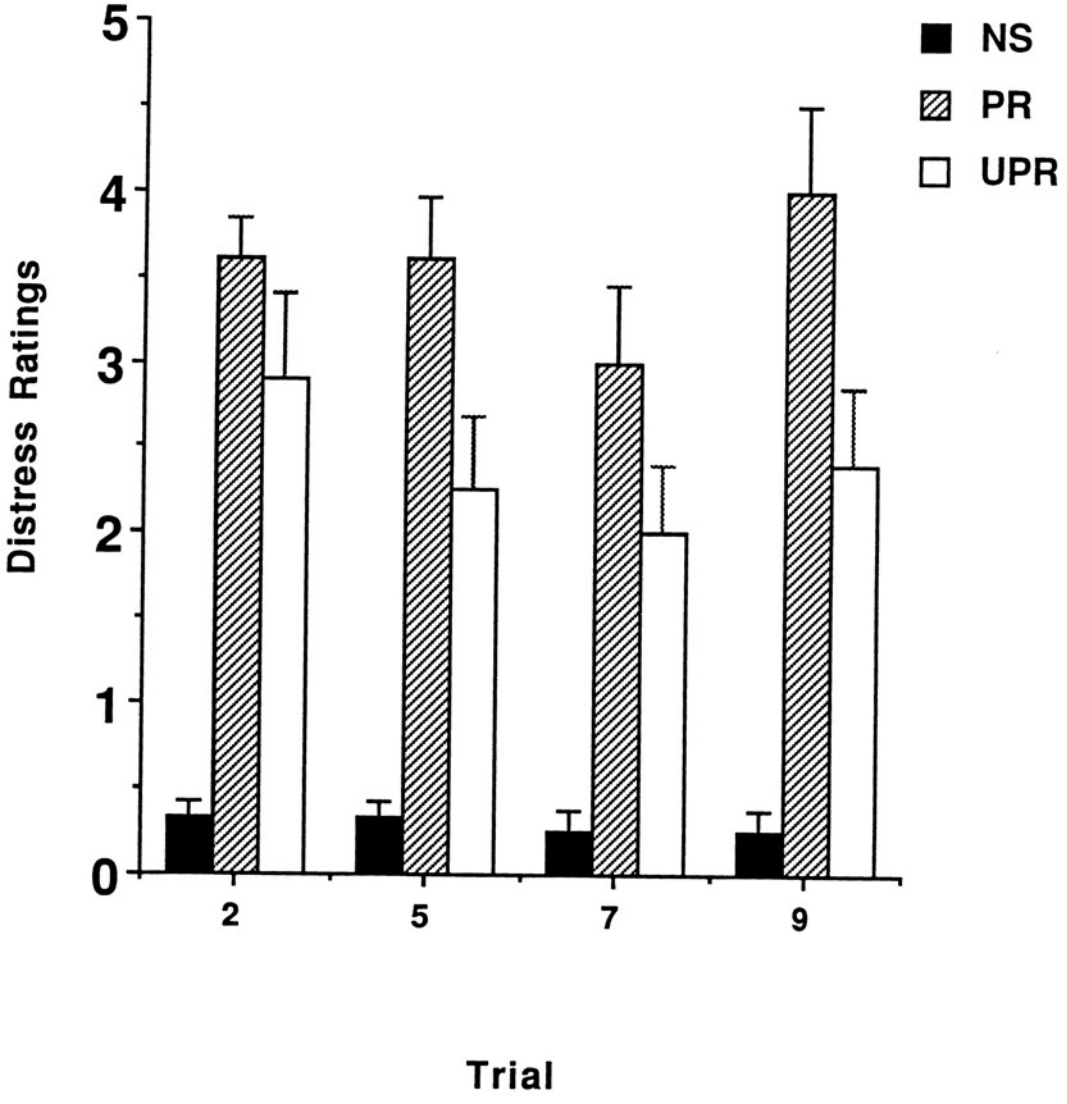


Figure caption 5: Mean systolic blood pressure changes from basal levels during the first and the second ten-minute task periods (task 1 and task 2). Each score is calculated by taking the average of five readings and subtracting the last three baseline measures taken before beginning of the tasks. Tukey post-hoc analyses revealed a significant difference between the UPR group and NS controls during the first task period.

Figure 5: SBP Change From Baseline

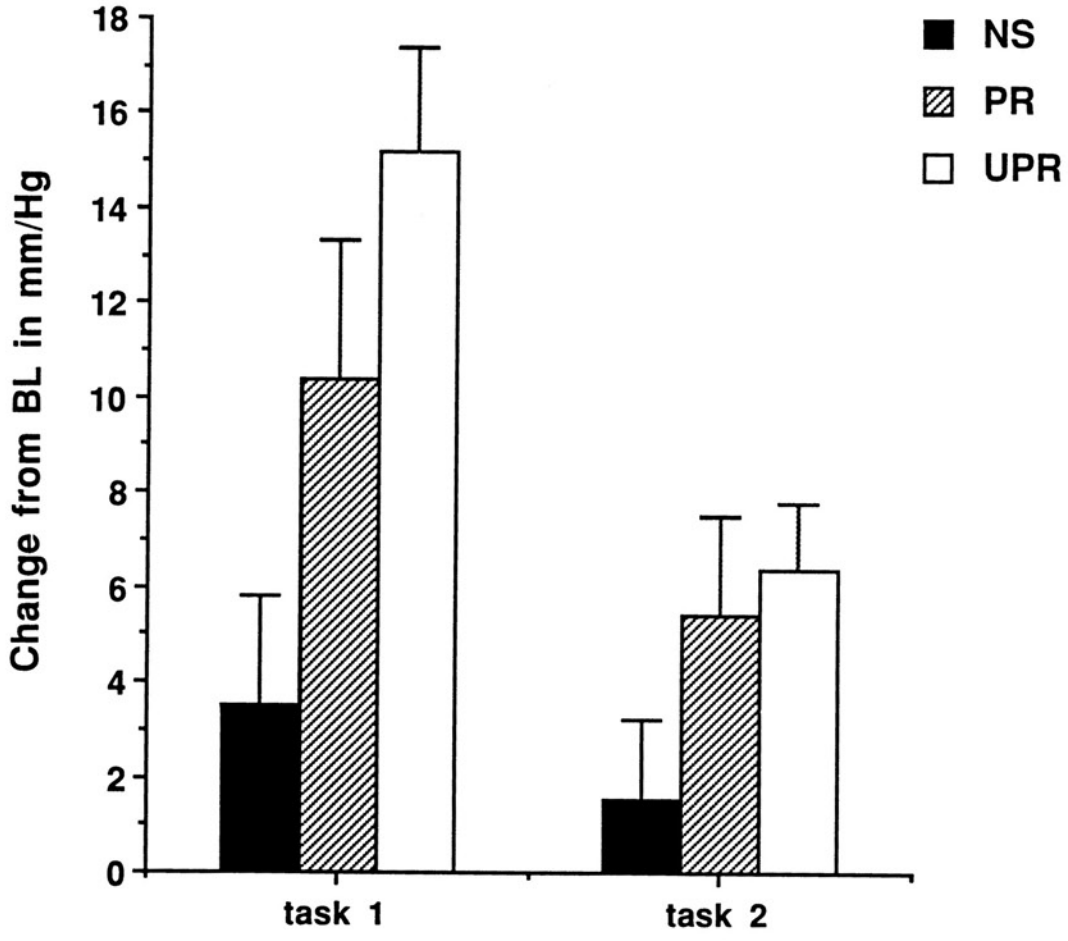


Figure caption 6: Systolic blood pressure changes from baseline levels for each of the ten readings taken throughout the tasks. Readings 9 to 13 were recorded during the first task period, and readings 14 to 18 during the second task period. Means are based on 21 subjects because of missing data.

Figure 6: SBP Change From Baseline (N=21)

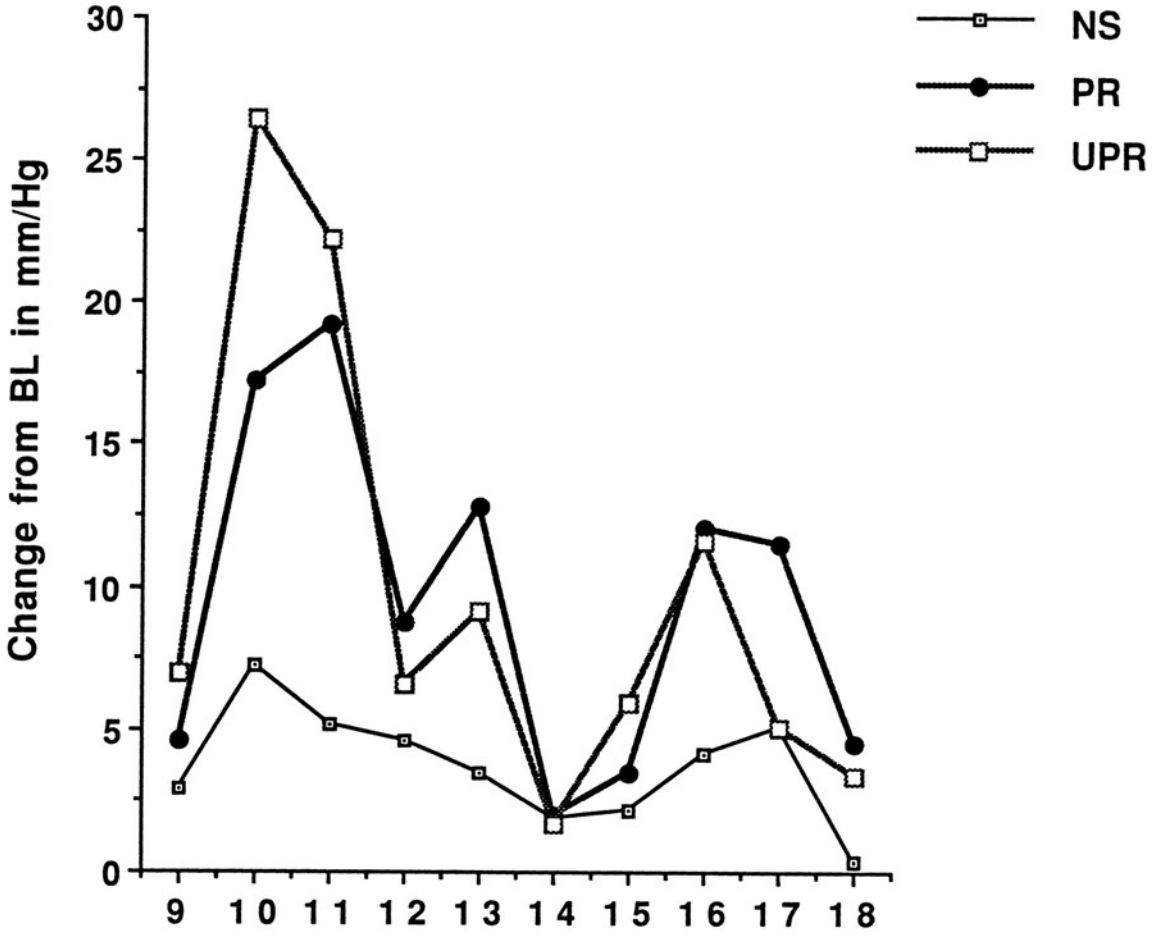


Figure caption 7: Mean diastolic blood pressure changes from basal levels during the first and the second ten-minute task periods (task 1 and task 2). Each score is calculated by taking the average of five readings and subtracting the last three baseline measures taken before beginning of the tasks. Tukey post-hoc analyses revealed a significant difference between the two stressor groups (PR and UPR) and NS controls during the first task period.

Figure 7: DBP Change From Baseline

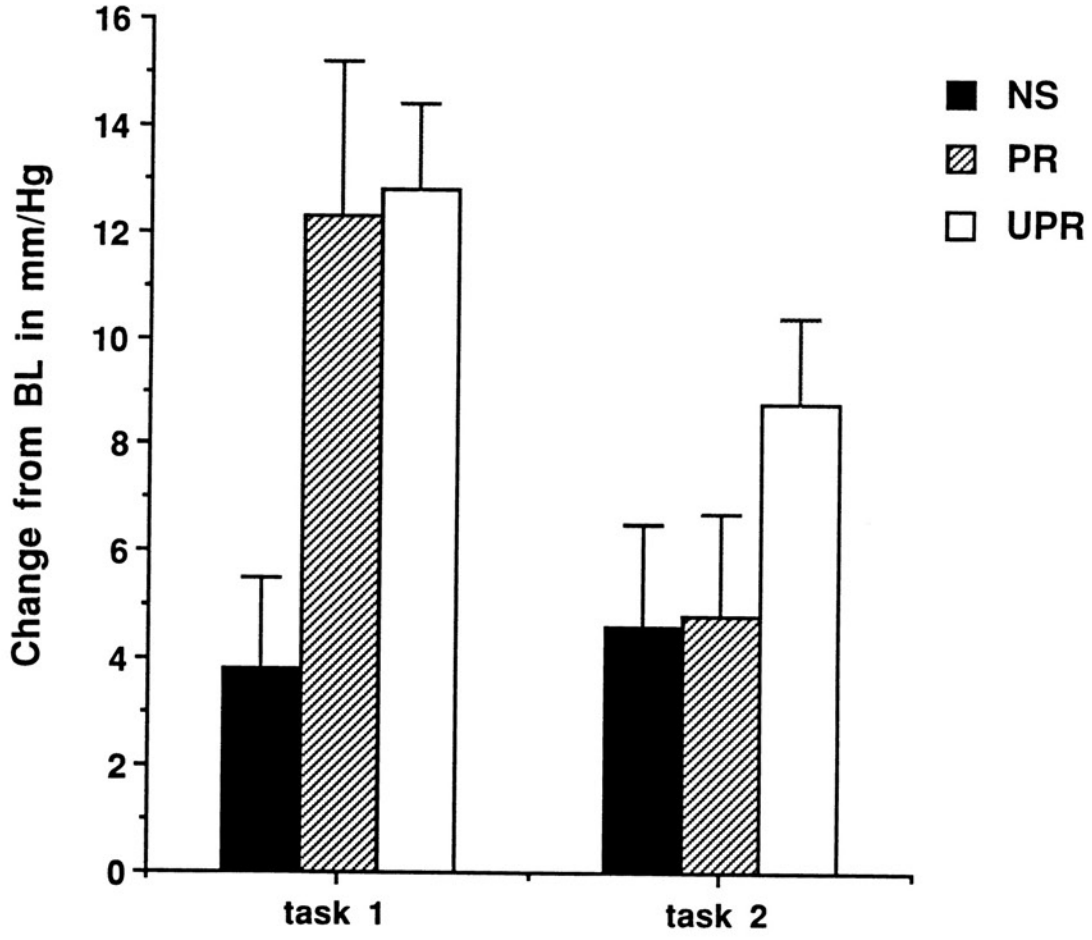


Figure caption 8: Diastolic blood pressure changes from baseline levels for each of the ten readings taken throughout the tasks. Readings 9 to 13 were recorded during the first task period, and readings 14 to 18 during the second task period. Means are based on 21 subjects because of missing data.

Figure 8: DBP Change From Baseline (N=21)

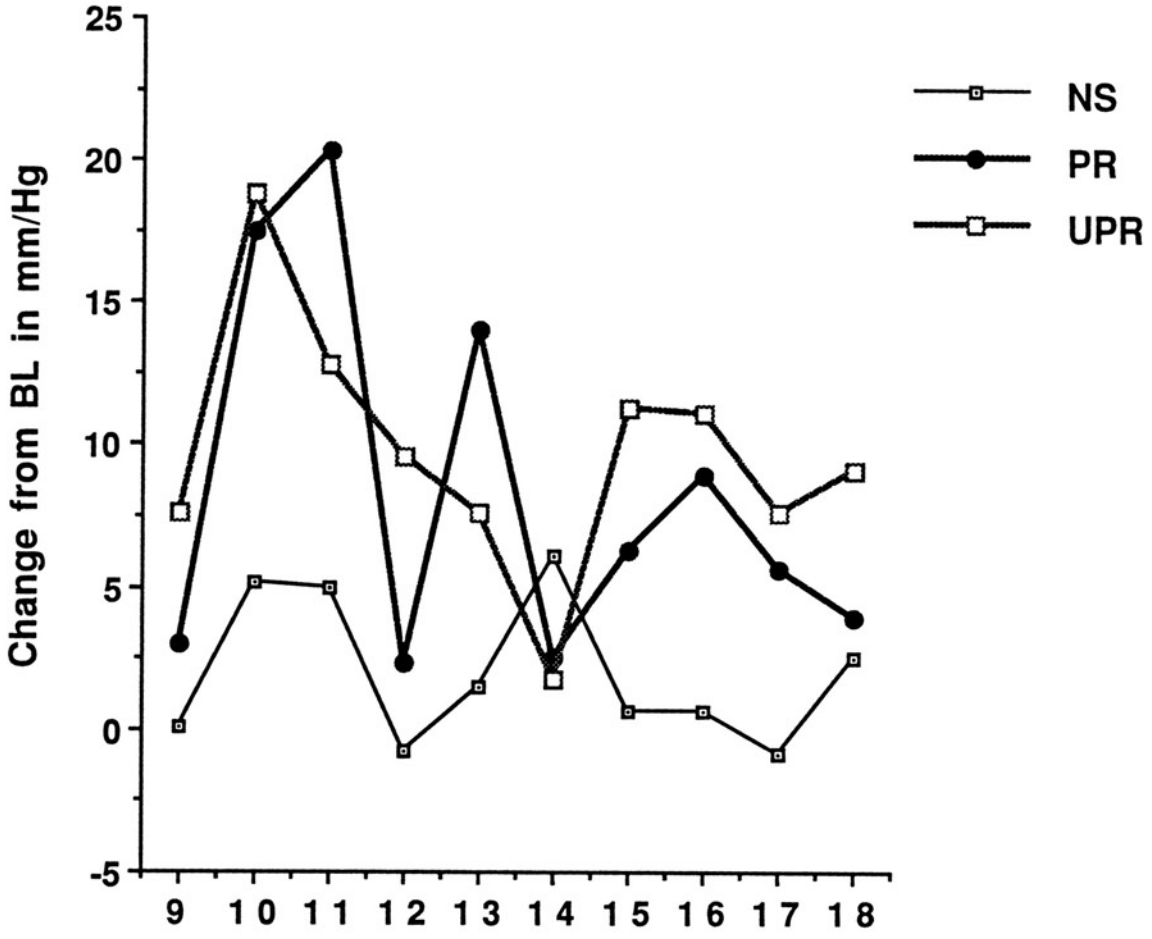


Figure caption 9: Mean heart rate changes from basal levels during the first and the second ten-minute task periods (task 1 and task 2). Each score is calculated by taking the average of five readings and subtracting the last three baseline measures taken before beginning of the tasks. Tukey post-hoc analyses revealed a significant difference for the PR group when compared to the NS and UPR groups during the first task period.

Figure 9: HR Change From Baseline

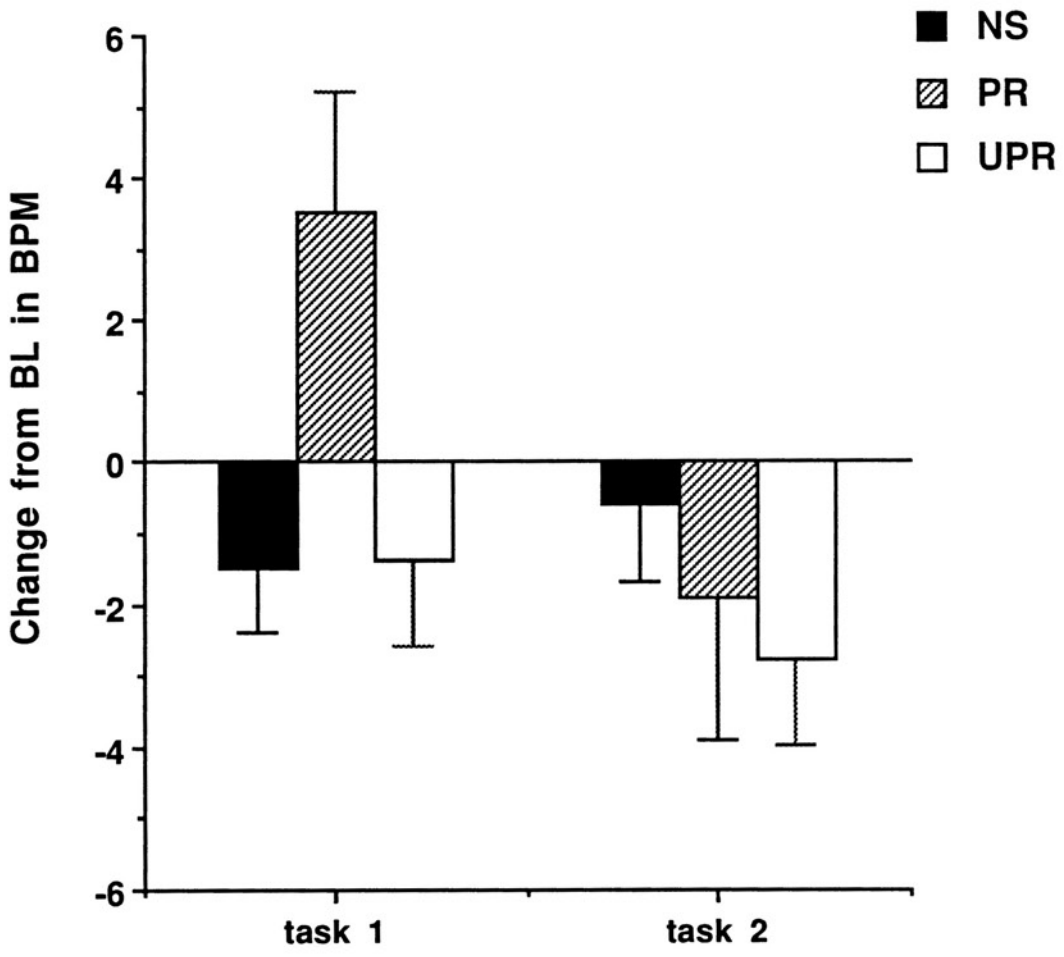


Figure caption 10: Heart rate changes from baseline levels for each of the ten readings taken throughout the tasks. Readings 9 to 13 were recorded during the first task period, and readings 14 to 18 during the second task period. Means are based on 21 subjects because of missing data.

Figure 10: HR Change From Baseline (N=20)

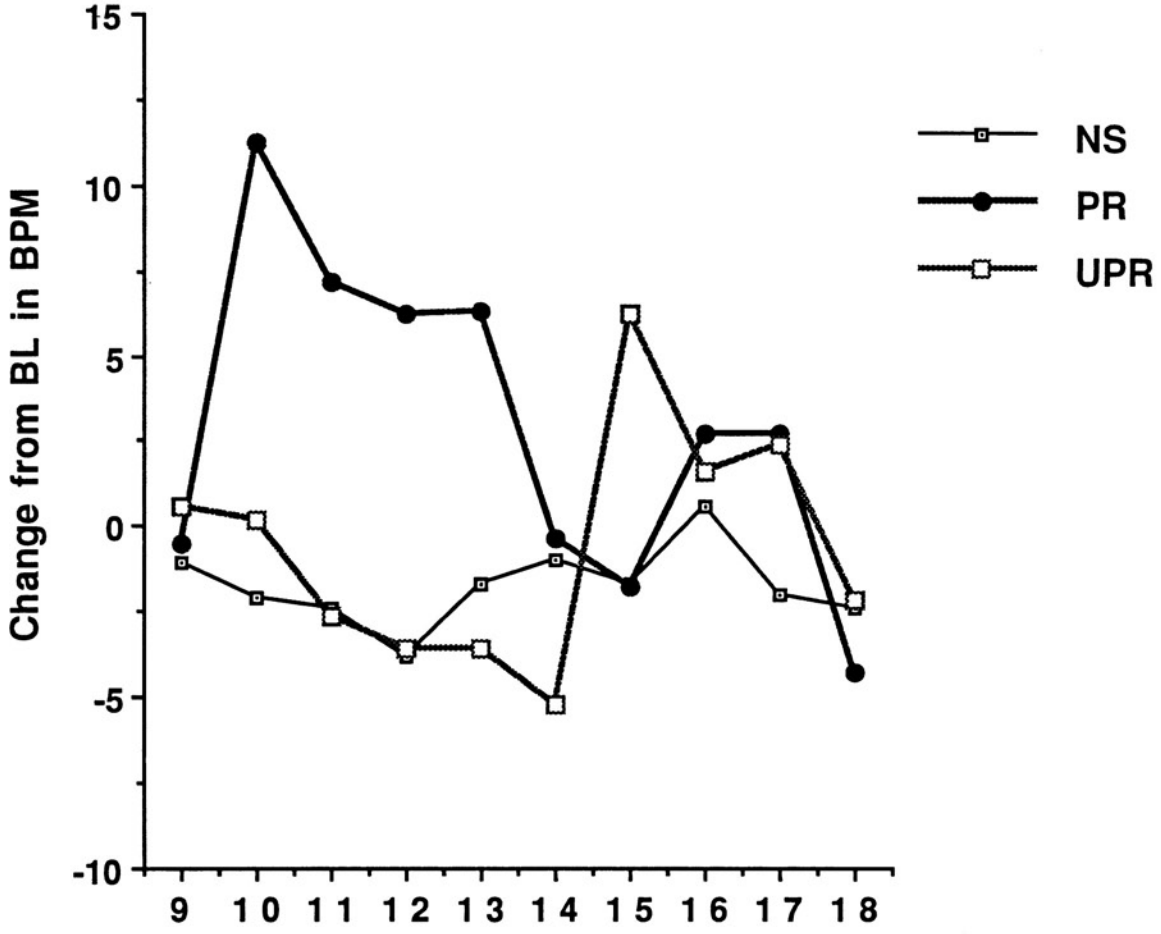


Figure caption 11: Mean changes in lymphocyte proliferation to Con A (10 ug/ml) from baseline levels. Values are shown in radioactive decays per minute (dpm) at the three blood sampling timepoints, after the first task period (task 1), after the second task period (task 2), and 20 minutes post-task (20 min.). Tukey post-hoc analyses showed a significant decrease in proliferation in the UPR group after the second task period.

Figure 11: Lymphocyte Proliferation to Con A (10 ug/ml)

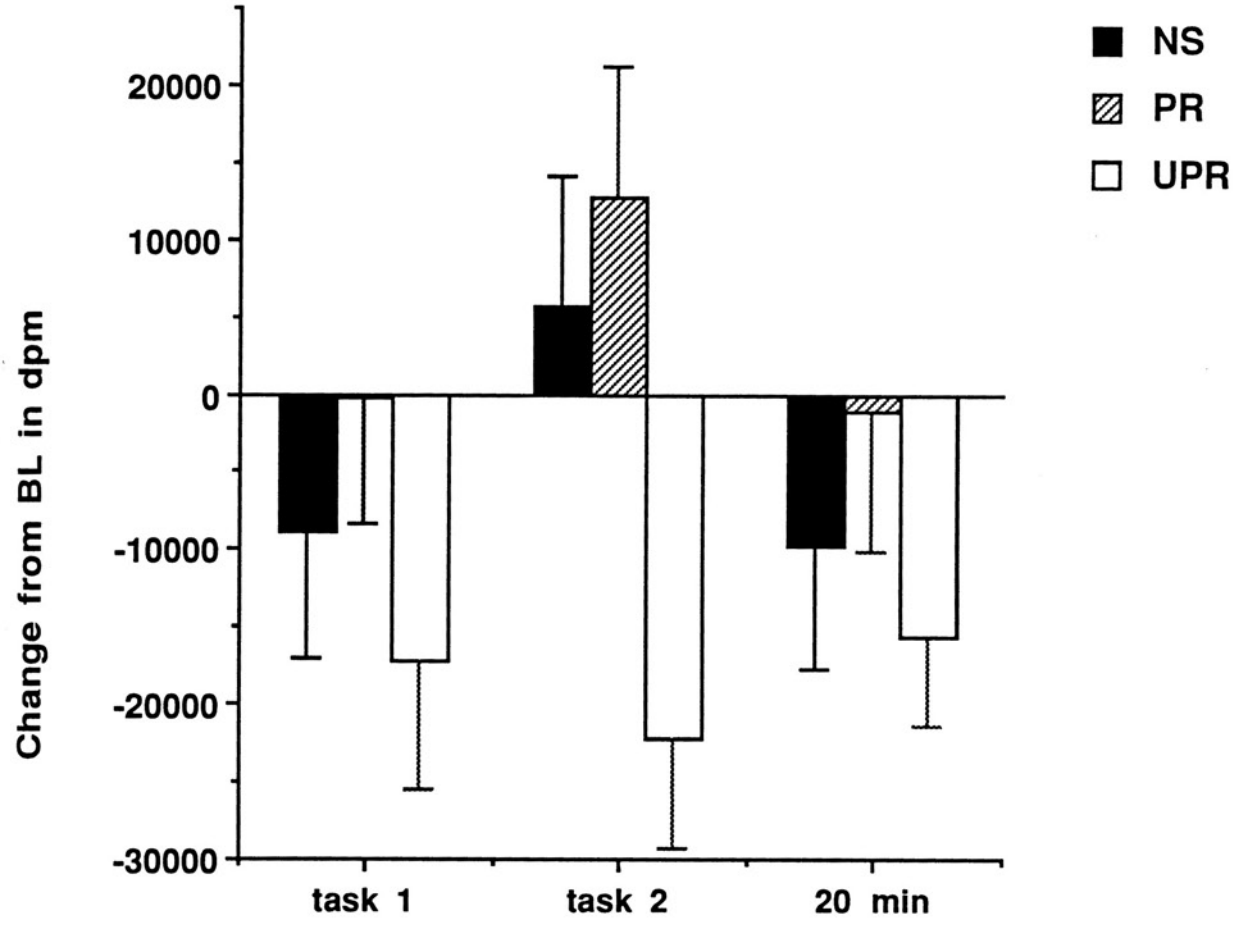


Figure caption 12: Mean total change in lymphocyte proliferation to Con A (10 ug/ml) from baseline levels. All three task timepoints were averaged and baseline levels subtracted to yield this total change score. Change is shown in decays per minute (dpm).

Figure 12: Mean Change in Lymphocyte Proliferation to Con A (10 ug/ml) (combining all timepoints)

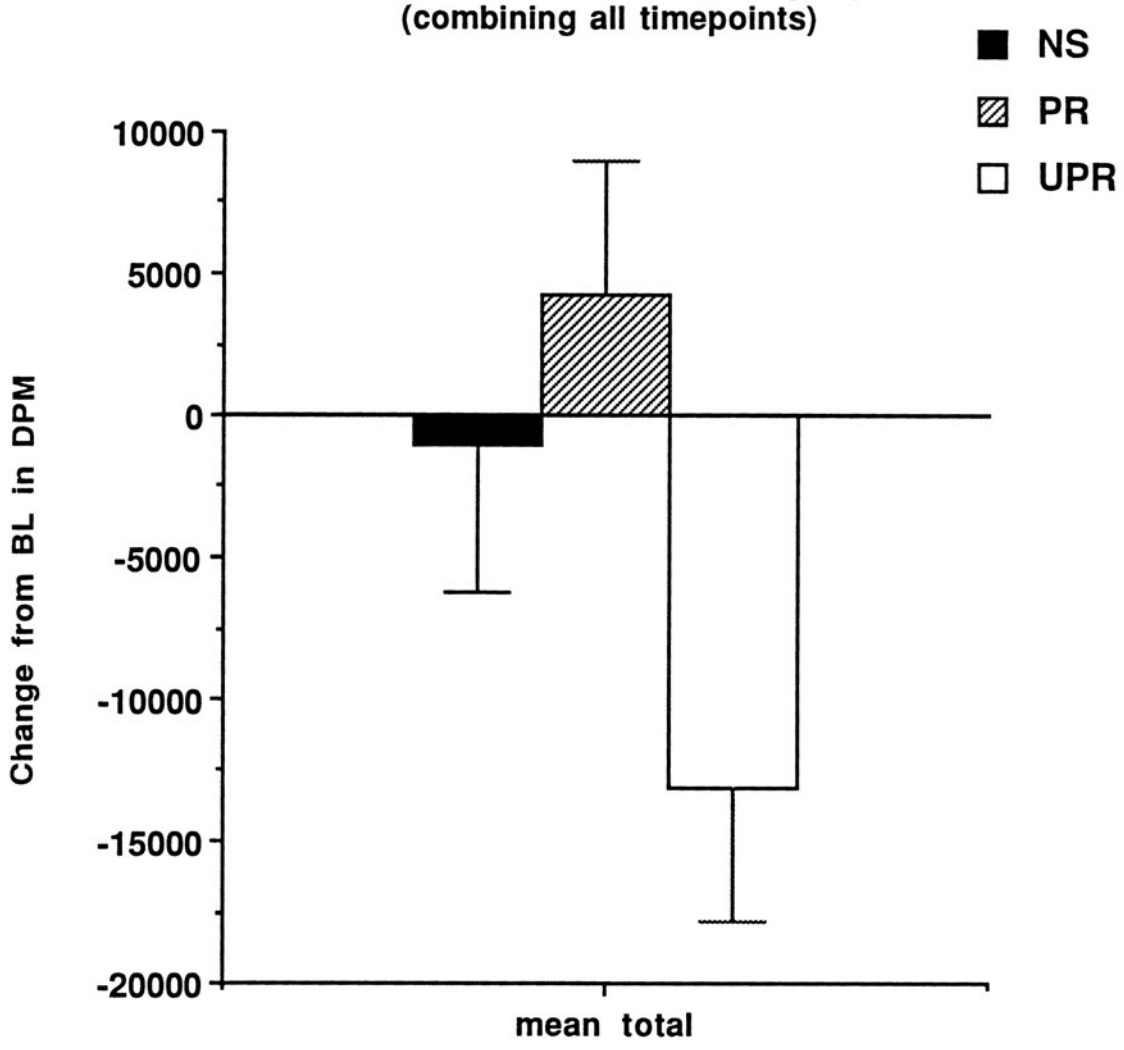


Figure caption 13: Mean changes in lymphocyte proliferation to PWM (.01 ug/ml) from baseline levels. Values are shown in radioactive decays per minute (dpm) at the three blood sampling timepoints, after the first task period (task 1), after the second task period (task 2), and 20 minutes post-task (20 min.). These changes were not statistically significant.

Figure 13: Lymphocyte Proliferation to PWM (.01 ug/ml)

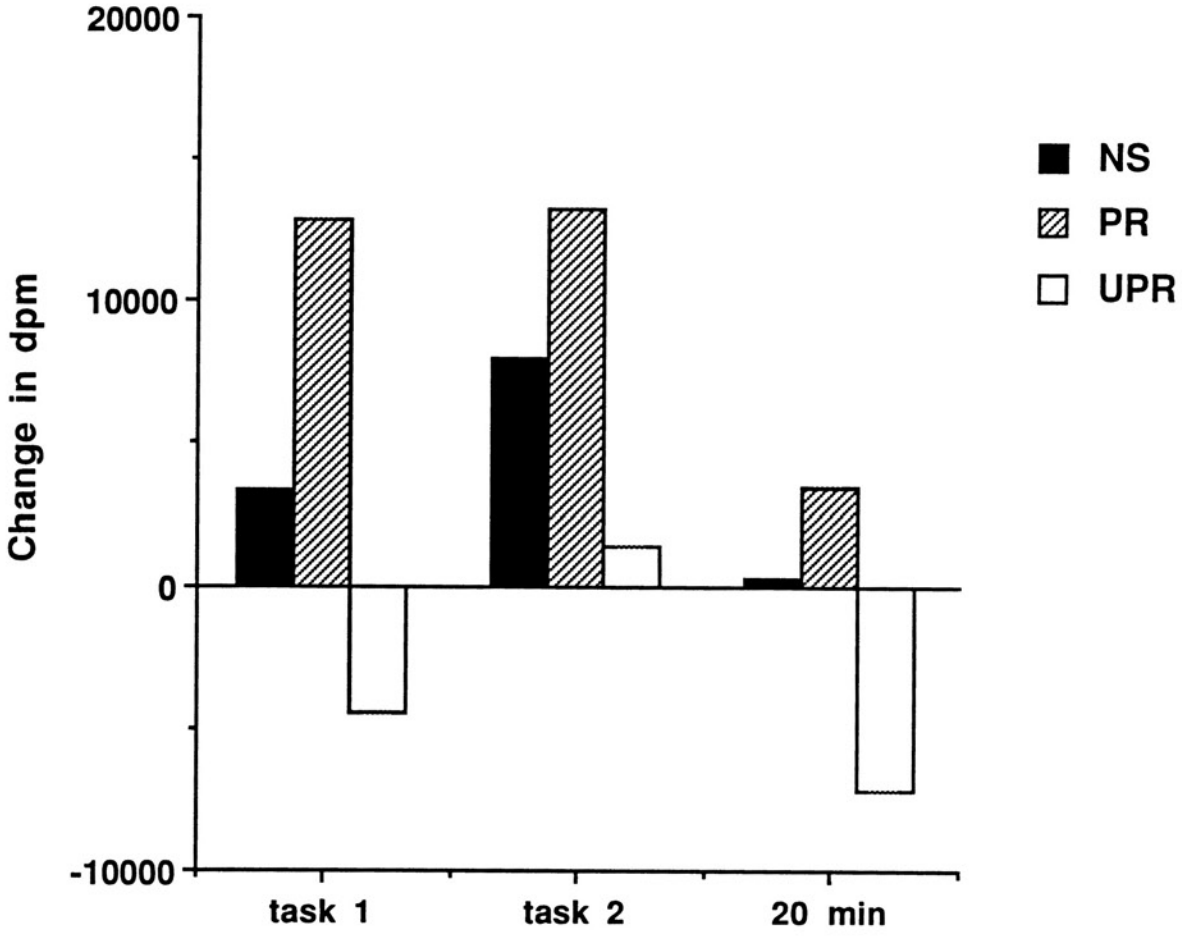
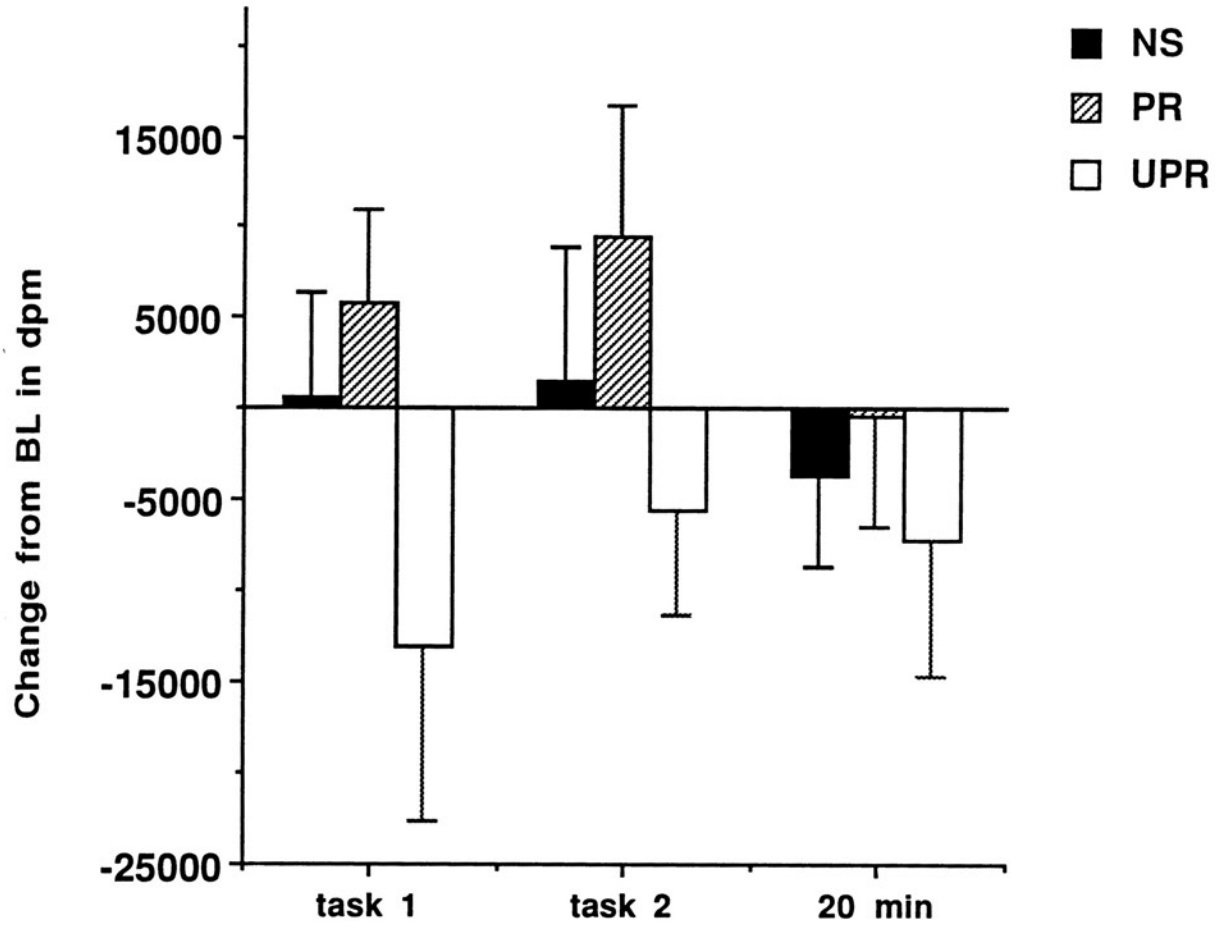


Figure caption 14: Mean changes in lymphocyte proliferation to PWM (.1 ug/ml) from baseline levels. Values are shown in radioactive decays per minute (dpm) at the three blood sampling timepoints, after the first task period (task 1), after the second task period (task 2), and 20 minutes post-task (20 min.). These changes were not statistically significant.

Figure 14: Lymphocyte Proliferation to PWM (0.1 ug/ml)



Appendix A: Consent form

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
F. EDWARD HÉBERT SCHOOL OF MEDICINE
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

MEDICAL PSYCHOLOGY

TEACHING HOSPITALS
WALTER REED ARMY MEDICAL CENTER
NAVAL HOSPITAL, BETHESDA
MALCOLM GROW AIR FORCE MEDICAL CENTER
WILFORD HALL AIR FORCE MEDICAL CENTER

CONSENT FOR RESEARCH PARTICIPATION

Please read carefully

Title of Study: The effects of task performance on physiological functioning.
Addendum to protocol RO7265: Conditioned Reactivity in Vietnam Veterans.

We are studying the effects of task performance on several psychological and physiological functions including coping, immune function, heart rate, blood pressure, and hormone level changes. In order to do this we will have you answer a number of questions and participate in some tasks. We are asking you to help us by participating. You will be scheduled for one 2 1/2-hour session in our laboratory. We will pay you $30 for participating in this session.

We are interested in getting to know you and evaluating some of your attitudes, beliefs, and personal characteristics. In order to accomplish this, we will ask you a number of questions concerning your background. We will ask you questions about your health and well-being and administer some tasks measuring mental performance. We may ask you to complete any of the following simple tasks: playing a video game, performing a cold pressor task (i.e. putting your hand in a basin with ice water or luke warm water), listening to tapes of music, performing a proofreading task, watching films depicting surgery or disease, tracing lines on a puzzle, working on a color-word coordination task or a mental arithmetic task.

During the time you are in the laboratory we will be measuring your heart rate and blood pressure. In order to do this we will attach 3 electrodes to your chest and a cuff like the one used in your doctor's office to your dominant arm. This cuff is attached to a machine that will cause the cuff to inflate automatically at approximately 2-3 minute intervals at certain times throughout the session.

We will also need to draw samples of your blood. The blood will be drawn by a trained phlebotomist. A butterfly needle will be inserted into a forearm vein and will remain in place during the laboratory session. We will take about 4-5 teaspoons (about 15 milliliters) of blood each time we withdraw blood. We will collect blood four times during the session.

If you have donated blood within the past week, we will not be able to draw blood from you. You will be in a sitting position when blood is drawn, and in the unlikely event of fainting, smelling salts and proper positioning will be used for reviving. You may observe bruising at the site of the blood draw. The discoloration may last a few weeks. The blood will provide us with useful information about physiological changes in response to task performance.

Possible inconvenience from this study involves possible frustration and discomfort during the tasks. The blood drawing may be discomforting. There may be some minor bruising and possible dizziness, but the individuals who will be drawing blood are highly qualified and trained to minimize any discomfort and problems associated with the procedure. If at any time during the study you should choose not to participate in some part of the study, you may do so without penalty.

If you decide to participate, you may withdraw or discontinue participation at any time for any reason without prejudice. If you have any questions, we expect you to ask us.

Research records of your participation in this study will be maintained by the principal investigator. Confidentiality is protected to the best extent possible under law. Your identity will not be traceable by anyone other than the principal investigator. When you have completed the session and we have coded your data or you have withdrawn from the study, your name will be deleted from all records and no one will be able to trace your data. The data will be published in scientific journals but will not be published in any manner that can identify you.

This study does not entail any physical or mental risk beyond those described above. If, however you should become uncomfortable during the study, sufficiently uncomfortable that you would like to end the session, tell us. We do not expect this to occur, but if, for any reason, you feel that continuing would constitute a hardship, please tell us and we will end the session.

If you believe that you have suffered any injury or illness as a result of participating in this research, please contact Research Administration, 295-3303, at the University. This office can review the matter with you and may be able to identify resources available to you. Information about possible judicial avenues of compensation is available from the University's Legal Counsel, 295-3028.

If you desire additional information about this experiment, either about the rationale for it or its findings, or about your rights as a participant, you may call the Department of Medical Psychology, 295-3270, to obtain information about it. In this way, you can make your participation in our research a more informative, educational experience. We welcome your comments and

suggestions, and appreciate you willingness to help us.

YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE. YOUR SIGNATURE INDICATES THAT, HAVING READ THE ABOVE INFORMATION, YOU HAVE DECIDED TO PARTICIPATE.

_____
Date signed

_____
Subject initials

_____
Signature of Subject

_____
Subject printed name

I was present during the explanation referred to above, as well as during the volunteer's opportunity to ask questions. I hereby witness the Volunteer's signature.

_____
Witness Signature

_____
Investigator or Designee signature

_____
Printed Name/SSN

_____
Printed Name/SSN

Appendix B: Screening questionnaires

TELEPHONE SCREEN

DATE:_____

NAME:_____

ADDRESS:_____

PHONE: (home)_____ (work)_____

Have you been in previous studies?

AGE:_____ Height _____ Weight _____

Occupation:_____

DO YOU PLAN ON MOVING IN THE NEXT 12 MONTHS: Y / N

DO YOU HAVE ANY PERMANENT OR CHRONIC HEALTH PROBLEMS: Y / N

EG. HIGH BP, ASTHMA, ALLERGIES, HEART CONDITION, ULCER, Raynaud's,
ARTHRITIS, DIABETES, CANCER, ..Cirr Pths, HSV _____

_____

OR ANY PROBLEMS WHICH HAVE LASTED FOR OVER 3 MONTHS: Y / N

IF YES, SPECIFY:_____

HAS YOUR HEALTH CHANGED IN THE LAST 6 MONTHS: Y / N

IF YES,HOW_____

DO YOU TAKE ANY PRESCRIPTION DRUGS: Y / N

IF YES, WHICH:_____

FOR WHAT HEALTH PROBLEMS:_____

DO YOU TAKE ANY NON-PERSCRIPTION DRUGS: Y / N

IF YES, WHICH:_____

FOR WHAT HEALTH PROBLEM:_____

DO YOU SMOKE: Y / N

IF YES, HOW MANY CIG./DAY:_____

DO YOU DRINK COFFEE OR CAFFEINATED SODA: Y / N

HOW MUCH A DAY:_____

DO YOU DRINK BEER OR WINE: Y / N

HOW MUCH A WEEK:_____

DO YOU DRINK ALCOHOLIC BEVERAGES OTHER THAN BEER OR WINE:Y/N

HOW MUCH A WEEK:_____

HAVE YOU EVER THOUGHT THAT YOU MIGHT HAVE A DRINKING PROBLEM:Y /N

DO YOU OR HAVE YOU EVER TAKEN DRUGS SUCH AS COCAINE, MARIJUANA, ETC: Y / N _____

ARE YOU CURRENTLY DIETING: Y / N

ARE YOU CURRENTLY CONSULTING A PSYCHOLOGIST OR PSYCHIATRIST:

Y / N IF YES, WHY:_____

DO YOU HAVE, OR HAVE YOU EVER HAD PROBLEMS SUCH AS DEPRESSION,ETC: Y / N_____

HAVE YOU EXPERIENCED ANY MAJOR LIFE EVENTS IN THE PAST 6 MONTHS (EG. MARRIAGE, DIVORCE, DEATH OF A FAMILY MEMBER OR CLOSE FRIEND, OTHER MAJOR CHANGES...): Y/N _____-

_____

subject no. _____
date _____

HEALTH FORM

Each of the following statements involves some aspect of how you rate your health. Please answer each item by circling the appropriate number on the 5-point scales. Consider the way you have felt only in the last 2 or 3 days. The numbers on the scale are illustrated below:

Not at all	A little bit	Moderately	Quite a bit	Extremely
1	2	3	4	5

IN THE LAST 2 OR 3 DAYS:

I have had symptoms of a cold or flu:
1 2 3 4 5

I have felt very tired and run down:
1 2 3 4 5

I have had a congested nose:
1 2 3 4 5

I have had headaches:
1 2 3 4 5

I have had a fever, chills or sensations of running a temperature:
1 2 3 4 5

I have had an upset stomach:
1 2 3 4 5

I have had a cough:
1 2 3 4 5

I have had body aches not associated with exercise:
1 2 3 4 5

****

In all I would rate my health in the last 2 or 3 days as:

1	2	3	4	5
much worse than usual	a bit worse than usual	same as usual	a bit better than usual	much better than usual

In the last 2 or 3 days I have felt as I have just caught a cold or flu:

YES NO

In the last 2 or three days I feel as I have just recovered from a cold or flu:

YES NO

In the last 2 or 3 days I have called a doctor to make an appointment or ask about my health:

YES NO

Appendix C: Questionnaires and Feather task

Extremely Painful

6

5

4

3

2

1

0

No Pain

Extremely Distressing

6

5

4

3

2

1

0

No Distress

INSTRUCTIONS

Below is a list of feelings that people sometimes have. Fill in one of the spaces on the right with a check that best describes HOW YOU ARE FEELING AT THIS MOMENT. Make only one check mark for each item.

(0) = not at all
(1) = a little
(2) = moderately
(3) = quite a bit
(4) = extremely

	(0)	(1)	(2)	(3)	(4)
1. feeling nervous or shaky inside					
2. feeling calm					
3. feeling faintness or dizziness					
4. feeling relaxed					
5. feeling pains in heart or chest					
6. feeling low in energy or slowed down					
7. feeling energetic					
8. trembling					
9. feeling rested					
10. feeling of being trapped or caught					
11. feeling suddenly scared					
12. feeling worried					
13. feeling at ease					
14. feeling fearful					
15. heart pounding or racing					
16. nausea or upset stomach					
17. hot or cold spells					
18. feeling comfortable					

	(0)	(1)	(2)	(3)	(4)
19. feeling nervous					
20. feeling you have a lump in your throat					
21. feeling pleasant					
22. feeling tense or keyed up					
23. spells of terror or panic					
24. feeling so restless you can't sit still					
25. feeling self-confident					
26. feeling helpless					

INSTRUCTIONS
Below is a list of feelings that people sometimes have. Fill in one of the spaces on the right with a check that best describes HOW YOU FELT DURING THE TASK. Make only one check mark for each item.

(0) = not at all
(1) = a little
(2) = moderately
(3) = quite a bit
(4) = extremely

	(0)	(1)	(2)	(3)	(4)
1. feeling nervous or shaky inside					
2. feeling calm					
3. feeling faintness or dizziness					
4. feeling relaxed					
5. feeling pains in heart or chest					
6. feeling low in energy or slowed down					
7. feeling energetic					
8. trembling					
9. feeling rested					
10. feeling of being trapped or caught					
11. feeling suddenly scared					
12. feeling worried					
13. feeling at ease					
14. feeling fearful					
15. heart pounding or racing					
16. nausea or upset stomach					
17. hot or cold spells					
18. feeling comfortable					

	(0)	(1)	(2)	(3)	(4)
19.feeling nervous					
20.feeling you have a lump in your throat					
21.feeling pleasant					
22.feeling tense or keyed up					
23.spells of terror or panic					
24.feeling so restless you can't sit still					
25.feeling self-confident					
26.feeling helpless					

For each of the following questions or statements please circle a number that best corresponds to how you feel about the task. The scales range from 0 to 6, 0 meaning you completely disagree and 6 meaning you completely agree with the statement.

1. During each trial were you able to predict when it (the trial) would end?

0 1 2 3 4 5 6
not at all very much

2. After each one of the trials, were you able to predict approximately how long the <u>following</u> trial would last?

0 1 2 3 4 5 6
not at all very much

3. Did the numbers on the tape help you judge how long each trial would last?

0 1 2 3 4 5 6
not at all very much

4. If you had to do this task again would you want to be told at the beginning of each trial how many seconds you will have to keep your hand in the water?

0 1 2 3 4 5 6
not at all very much

5. How much control did you feel you had over what happened to you during the tasks?

0 1 2 3 4 5 6
none at all very much

6. How stressed did you feel during the tasks?

0 1 2 3 4 5 6
not at all very much

7. What did you do or think about when you had your hand in the water? Check <u>all</u> the items that apply to you:

___ I tried to think about pleasant memories.
___ I tried to focus on the sensations in my hand.
___ I tried to forget about the sensations in my hand.
___ I tried to figure out how much longer I would have to keep my hand in the water.
___ I did not want to know how much longer I would have to keep my hand in the water.
___ I thought about how I could get more information on how long the next trials would last.
___ I tried to tune out what was happening in the room.
___ I listened closely to the tape.
___ I looked around for clues to get more information about the task.
___ I tried to relax.

Below you will find a series of statements. Please read each statement carefully and respond to it by expressing the extent to which you believe the statement applies to you. For all items a response from 1 to 7 is required. Use the number that best reflects your belief when the scale is defined as follows.

1. The statement doesn't apply to me at all.
2. The statement usually doesn't apply to me.
3. Most often the statement does not apply.
4. I am unsure about whether or not the statement applies to me, or it applies to me about half the time.
5. The statement applies more often than not.
6. The statement usually applies to me.
7. The statement always applies to me.

It is important that you respond to all items.

1. I prefer a job where I have a lot of control over what I do and when I do it.

   1 2 3 4 5 6 7

2. I enjoy political participation because I want to have as much of a say in running government as possible.

   1 2 3 4 5 6 7

3. I try to avoid situations where someone else tells me what to do.

   1 2 3 4 5 6 7

4. I would prefer to be a leader rather than a follower.

   1 2 3 4 5 6 7

5. I enjoy being able to influence the actions of others.

   1 2 3 4 5 6 7

6. I am careful to check everything on an automobile before I leave for a long trip.

   1 2 3 4 5 6 7

7. Others usually know what is best for me.

   1 2 3 4 5 6 7

8 I enjoy making my own decisions.

   1 2 3 4 5 6 7

9. I enjoy having control over my own destiny.

   1 2 3 4 5 6 7

10. I would rather someone else took over the leadership role when I'm involved in a group project.

1 2 3 4 5 6 7

11. I consider myself to be generally more capable of handling situations than others are.

1 2 3 4 5 6 7

12. I'd rather run my own business and make my own mistakes than listen to someone else's orders.

1 2 3 4 5 6 7

13. I like to get a good idea of what a job is all about before I begin.

1 2 3 4 5 6 7

14. When I see a problem I prefer to do something about it rather than sit by and let it continue.

1 2 3 4 5 6 7

15. When it comes to orders, I would rather give them than receive them.

1 2 3 4 5 6 7

16. I wish I could push many of life's daily decisions off on someone else.

1 2 3 4 5 6 7

17. When driving, I try to avoid putting myself in a situation where I could be hurt by someone else's mistake.

1 2 3 4 5 6 7

18. I prefer to avoid situations where someone else has to tell me what it is I should be doing.

1 2 3 4 5 6 7

19. There are many situations in which I would prefer only one choice rather than having to make a decision.

1 2 3 4 5 6 7

20. I like to wait and see if someone else is going to solve a problem so that I don't have to be bothered by it.

1 2 3 4 5 6 7

21. When I go out with other people I usually make most of the arrangements.

1 2 3 4 5 6 7

22. I am comfortable lending my possessions (e.g., books and records) to my friends.

1 2 3 4 5 6 7

23. If I am going to an event (a lecture or movie) which I expect will be crowded, I try to arrive early.

1 2 3 4 5 6 7

24. I almost never get things done until the last minute.

1 2 3 4 5 6 7

25. I like to gamble and play games of chance.

1 2 3 4 5 6 7

26. I would rather play an individual sport such as tennis than a team sport such as basketball.

1 2 3 4 5 6 7

27. I would prefer to get on a subway or bus early and have a longer ride but a choice of where to sit than to have a shorter ride and less choice.

1 2 3 4 5 6 7

28. I don't mind other people scheduling my time.

1 2 3 4 5 6 7

29. I really get a kick out of driving a very responsive car.

1 2 3 4 5 6 7

30. I think it would be fun to be hypnotized.

1 2 3 4 5 6 7

31. I like to get high on alcohol or drugs.

1 2 3 4 5 6 7

32. I usually push an elevator button even if it is lighted indicating that someone has already pushed it.

1 2 3 4 5 6 7

RECENT LIFE CHANGES QUESTIONNAIRE

I. Instructions for Marking Your Recent Life Changes

If the event in question has occurred to you within the past three months mark an "X" in the column to the right of the question. If the event has not occurred to you during the last three months, leave the column empty.

Now go through the questionnaire and mark your recent life changes. The column marked "Your Adjustment Score" will be explained at the end of the questionnaire.

A. HEALTH

within the time period listed, have you experienced:

	0-3 months ago	Your Adjustment Score
1. an illness or injury which:		
(a) kept you in bed a week or more, or took you to the hospital?	____	____
(b) was less serious than described above?	____	____
2. a major change in eating habits?	____	____
3. a major change in sleeping habits?	____	____
4. a change in your usual type and/or amount of recreation?	____	____
5. major dental work?	____	____

B. WORK

	0-3 months ago	Your Adjustment Score
6. changed to a new type of work?	____	____
7. changed your work hours or conditions?	____	____

B. WORK

within the time period listed, have you experienced:

	0-3 months ago	Your Adjustment Score
8. had a change in your responsibilities at work?	_____	_____
(a) more responsibilities?	_____	_____
(b) less responsibilities?	_____	_____
(c) promotion?	_____	_____
(d) demotion?	_____	_____
(e) transfer?	_____	_____
9. experienced troubles at work?	_____	_____
10. experienced a major business readjustment?	_____	_____
11. retired?	_____	_____
12. experienced being:		
(a) fired from work?	_____	_____
(b) laid off from work?	_____	_____
13. taken courses by mail or studied at home to help you in your work?	_____	_____

C. HOME AND FAMILY

within the time periods listed, have you experienced:

	0-3 months ago	Your Adjustment Score
14. a change in residence:		
(a) a move within the same town or city?	_____	_____
(b) a move to a different town, city, or state?	_____	_____
15. a change in family "get-togethers"?	_____	_____
16. a major change in the health or behavior of a family member (illnesses, accidents, drug or disciplinary problems, etc.)?	_____	_____

within the time periods listed, have you experienced:

	0-3 months ago	Your Adjustment Score
17. the death of a spouse?	____	____
18. the death of a:		
(a) child?	____	____
(b) brother or sister?	____	____
(c) parent?	____	____
(d) other close family member?	____	____
19. the death of a close friend?	____	____
20. a change in the marital status of your parents:		
(a) divorce?	____	____
(b) remarriage?	____	____

NOTE:
(Questions 21-32 concern marriage. For persons never married, go to item 34.)

within the time periods listed, have you experienced?

	0-3 months ago	Your Adjustment Score
21. marriage?	____	____
22. a change in arguments with your spouse?	____	____
23. in-law problems?	____	____
24. a separation from spouse:		
(a) due to work?	____	____
(b) due to marital problems?	____	____
25. a reconciliation with spouse?	____	____
26. a divorce?	____	____
27. a gain of a new family member:		
(a) birth of a child?	____	____
(b) adoption of a child?	____	____
(c) a relative moving in with you?	____	____
28. spouse beginning or ceasing work outside the home?	____	____

within the time periods listed, have you experienced:

	0-3 months ago	Your Adjustment Score
29. wife (or self) becoming pregnant?	____	____
30. a child leaving home:		
(a) due to marriage?	____	____
(b) to attend college?	____	____
(c) for other reasons?	____	____
31. wife or (self) having a miscarriage or an abortion?	____	____
32. birth of a grandchild?	____	____

D. PERSONAL AND SOCIAL

within the time periods listed, have you experienced:

33. a major personal achievement?	____	____
34. a change in your personal habits (your dress, friends life-style, etc.)?	____	____
35. sexual difficulties?	____	____
36. beginning or ceasing school or college?	____	____
37. a change of school or college?	____	____
38. a vacation?	____	____
39. a change in your religious beliefs?	____	____
40. a change in your social activities (clubs, movies, visiting)?	____	____
41. a minor violation of the law?	____	____
42. legal troubles resulting in your being held in jail?	____	____
43. a change in your political beliefs?	____	____
44. a new, close, personal relationship?	____	____
45. an engagement to marry?	____	____

within the time periods listed, have you experienced?

	0-3 months ago	Your Adjustment Score
46. a "falling out" of a close personal relationship?	_____	_____
47. girlfriend (or boyfriend) problems?	_____	_____
48. a loss or damage of personal property?	_____	_____
49. an accident?	_____	_____
50. a major decision regarding your immediate future?	_____	_____

L. FINANCIAL

within the time periods listed, have you:

51. taken on a moderate purchase, such as a T.V., car, freezer?	_____	_____
52. taken on a major purchase or a mortgage loan, such as a home, business, property?	_____	_____
53. experienced a foreclosure on a mortgage or loan?	_____	_____
54. experienced a major change in finances:		
(a) increased income?	_____	_____
(b) decreased income?	_____	_____
(c) credit rating difficulties?	_____	_____

INSTRUCTIONS FOR SCORING YOUR ADJUSTMENT TO
TO YOUR RECENT LIFE CHANGE

Persons adapt to their recent life changes in different ways. Some people find the adjustment to a residential move, for example, to be enormous, while others find very little life adjustment necessary. You are now requested to "score" each of the recent life changes that you marked with an "X" as to the amount of adjustment you needed to handle the event.

Your scores can range from 1 to 100 "points." If, for example, you experienced a recent residential move but felt it required very little life adjustment, you would choose a low number and place it in the blank to the right of the question's boxes. On the other hand, if you recently changed residence and felt it required a near maximal life adjustment, you would place a high number, toward 100, in the blank to the right of that question's boxes. For intermediate life adjustment scores you would choose intermediatge numbers between 1 and 100.

Please go back through your questionnaire and for each recent life change you indicated with an "X," choose your personal life change adjustment score (between 1 and 100) which reflects what you saw to be the amount of life adjustment necessary to cope with or handle the event. Use both your estimates of the intensity of the life change and its duration to arrive at your scores.

THE HASSLES SCALE

Directions: Hassles are irritants that can range from minor annoyances to fairly major pressures, problems, or difficulties. They can occur few or many times.

Listed in the center of the following pages are a number of ways in which a person can feel hassled. First, circle the hassles that have happened to you in the past month. Then look at the numbers on the right of the items you circled. Indicate by circling a 1, 2, or 3 how SEVERE each of the circled hassles has been for you in the past month. If a hassle did not occur in the last month do NOT circle it.

HASSLES	SEVERITY 1. Somewhat severe 2. Moderately severe 3. Extremely severe		
(1) Misplacing or losing things	1	2	3
(2) Troublesome neighbors	1	2	3
(3) Social obligations	1	2	3
(4) Inconsiderate smokers	1	2	3
(5) Troubling thoughts about your future	1	2	3
(6) Thoughts about death	1	2	3
(7) Health of a family member	1	2	3
(8) Not enough money for clothing	1	2	3
(9) Not enough money for housing	1	2	3
(10) Concerns about owing money	1	2	3

HASSLES	SEVERITY 1. Somewhat severe 2. Moderately severe 3. Extremely severe		
(11) Concerns about getting credit	1	2	3
(12) Concerns about money for emergencies	1	2	3
(13) Someone owes you money	1	2	3
(14) Financial responsibility for someone who doesn't live with you	1	2	3
(15) Cutting down on electricity, water, etc.	1	2	3
(16) Smoking too much	1	2	3
(17) Use of alcohol	1	2	3
(18) Personal use of drugs	1	2	3
(19) Too many responsibilities	1	2	3
(20) Decisions about having children	1	2	3
(21) Non-family members living in your house	1	2	3
(22) Care for pet	1	2	3
(23) Planning meals	1	2	3
(24) Concerned about the meaning of life	1	2	3
(25) Trouble relaxing	1	2	3
(26) Trouble making decisions	1	2	3
(27) Problems getting along with fellow workers	1	2	3
(28) Customers or clients give you a hard time	1	2	3
(29) Home maintenance (inside)	1	2	3
(30) Concerns about job security	1	2	3
(31) Concerns about retirement	1	2	3
(32) Laid off or out of work	1	2	3

SEVERITY

1. Somewhat severe
2. Moderately severe
3. Extremely severe

	HASSLES			
(33)	Don't like current work duties	1	2	3
(34)	Don't like fellow workers	1	2	3
(35)	Not enough money for basic necessities	1	2	3
(36)	Not enough money for food	1	2	3
(37)	Too many interruptions	1	2	3
(38)	Unexpected company	1	2	3
(39)	Too much time on hands	1	2	3
(40)	Having to wait	1	2	3
(41)	Concerns about accidents	1	2	3
(42)	Being lonely	1	2	3
(43)	Not enough money for health care	1	2	3
(44)	Fear of confrontation	1	2	3
(45)	Financial security	1	2	3
(46)	Silly practical mistakes	1	2	3
(47)	Inability to express yourself	1	2	3
(48)	Physical illness	1	2	3
(49)	Side effects of medication	1	2	3
(50)	Concerns about medical treatment	1	2	3
(51)	Physical appearance	1	2	3
(52)	Fear of rejection	1	2	3
(53)	Difficulties with getting pregnant	1	2	3
(54)	Sexual problems that result from physical problems	1	2	3

SEVERITY

1. Somewhat severe
2. Moderately severe
3. Extremely severe

	HASSLES			
(55)	Sexual problems other than those resulting from physical problems	1	2	3
(56)	Concerns about health in general	1	2	3
(57)	Not seeing enough people	1	2	3
(58)	Friends or relatives too far away	1	2	3
(59)	Preparing meals	1	2	3
(60)	Wasting time	1	2	3
(61)	Auto maintenance	1	2	3
(62)	Filling out forms	1	2	3
(63)	Neighborhood deterioration	1	2	3
(64)	Financing children's education	1	2	3
(65)	Problems with employees	1	2	3
(66)	Problems on job due to being a woman or man	1	2	3
(67)	Declining physical abilities	1	2	3
(68)	Being exploited	1	2	3
(69)	Concerns about bodily functions	1	2	3
(70)	Rising prices of common goods	1	2	3
(71)	Not getting enough rest	1	2	3
(72)	Not getting enough sleep	1	2	3
(73)	Problems with aging parents	1	2	3
(74)	Problems with your children	1	2	3
(75)	Problems with persons younger than yourself	1	2	3
(76)	Problems with your lover	1	2	3

	HASSLES	SEVERITY 1. Somewhat severe 2. Moderately severe 3. Extremely severe		
(77)	Difficulties seeing or hearing	1	2	3
(78)	Overloaded with family responsibilities	1	2	3
(79)	Too many things to do	1	2	3
(80)	Unchallenging work	1	2	3
(81)	Concerns about meeting high standards	1	2	3
(82)	Financial dealings with friends or acquaintance.	1	2	3
(83)	Job dissatisfactions	1	2	3
(84)	Worries about decisions to change jobs	1	2	3
(85)	Trouble with reading, writing, or spelling abilities	1	2	3
(86)	Too many meetings	1	2	3
(87)	Problems with divorce or separation	1	2	3
(88)	Trouble with arithmetic skills	1	2	3
(89)	Gossip	1	2	3
(90)	Legal problems	1	2	3
(91)	Concerns about weight	1	2	3
(92)	Not enough time to do the things you need to do.	1	2	3
(93)	Television	1	2	3
(94)	Not enough personal energy	1	2	3
(95)	Concerns about inner conflicts	1	2	3
(96)	Feel conflicted over what to do	1	2	3
(97)	Regrets over past decisions	1	2	3
(98)	Menstrual (period) problems	1	2	3
(99)	The weather	1	2	3
(100)	Nightmares	1	2	3

	HASSLES	SEVERITY 1. Somewhat severe 2. Moderately severe 3. Extremely severe		
(101)	Concerns about getting ahead	1	2	3
(102)	Hassles from boss or supervisor	1	2	3
(103)	Difficulties with friends	1	2	3
(104)	Not enough time for family	1	2	3
(105)	Transportation problems	1	2	3
(106)	Not enough money for transportation	1	2	3
(107)	Not enough money for entertainment and recreation	1	2	3
(108)	Shopping	1	2	3
(109)	Prejudice and discrimination from others	1	2	3
(110)	Property, investments or taxes	1	2	3
(111)	Not enough time for entertainment and recreation	1	2	3
(112)	Yardwork or outside home maintenance	1	2	3
(113)	Concerns about news events	1	2	3
(114)	Noise	1	2	3
(115)	Crime	1	2	3
(116)	Traffic	1	2	3
(117)	Pollution	1	2	3
	HAVE WE MISSED ANY OF YOUR HASSLES? IF SO, WRITE THEM IN BELOW:			
(118)	_____	1	2	3

ONE MORE THING: HAS THERE BEEN A CHANGE IN YOUR LIFE THAT AFFECTED HOW YOU ANSWERED THIS SCALE? IF SO, TELL US WHAT IT WAS:

_____

Subject # _____

FOOD CHECKLIST

Please circle any of the following items which you consumed **during the** last 12-hour period.

Coffee number of cups_____

Tea number of cups_____

Cola number of cups_____

Chocolate, cocoa, wine, beer/alcohol, decaffeinated coffee.

Breads containing raisins, prunes, orange peel, banana or pineapple.

Cheese bread, nut bread containing walnuts.

Raisin bran.

Desserts containig walnuts, sour cream or fruits, (e.g. fruit cake, plum pudding, mince pie.....)

Banana, avocado, pineapple, canned figs, raisins, plums and prunes.

Oranges, orange juice, fruit cocktail with pineapple.

Tomato, broad beans (fava beans), eggplant or any vegetable in cheesesauce.

Chicken liver, herring, smoked or pickled fish, brain, aged cheese, sour cream, anchovies.

Cheese, omelets, spanish omelets with aged cheese.

Macaroni and cheese, spaghetti with tomato sauce.

Walnuts, chocolate or coffee flavored candy, candy containing walnuts. Catsup, chili sauce, olives, vanilla.

Eggs, Dairy products (e.g. milk, cheese, yogurt,...), red meat (incl. pork).

Subject #_____.

1. Do you exercise regularly? **yes / no**

2. How many hours a day, on the average, do you usually spend exercising (e.g. running, aerobics, swimming, playing sports, walking,...)?_____

3. How many hours did you spend exercising in the past 24 hours?_____

4. Have you been suffering from any conditions which might be influencing the way you feel? Please circle any of the following: **Cold, hangover, nausea, vomiting, cold sores, backaches, sleeplessness, fatigue, diarrhea, chest pain, other (please specify):**_____

5. Are you under any particular stress today, or are you expecting any particular stress today? (e.g. argued with a friend, family member ill, expecting a very stressful day at work,...) If so, please describe:

_____

6. How many hours do you usually sleep each night?_____

7. How many hours did you sleep last night?_____

8. How well did you sleep last night? (circle a number)

very well 1 2 3 4 5 6 7 very badly

9. Overall, how do you feel today?

very well 1 2 3 4 5 6 7 very badly

10. How much alcohol did you drink in the past 12 hours? (number of drinks) _____

11. How many cups of caffeinated coffee or tea did you drink this morning? _____

The following questions refer to your eating habits.
For each of the questions circle the number next to the answer that most applies to you.

1) How often do you eat breakfast?

0 = didn't do this at all during the past year
1 = did this occasionally, but less than once a month
2 = did this once a month or more
3 = did this once a week or more
4 = did this daily or almost daily

2) How often do you take vitamin supplements?

0 = never or occasionally (less than once a month)
1 = about once a week
2 = about two or three times a week
3 = about once a day
4 = more than once a ~~week~~ day

3) How often do you eat fruit (for example, apples, pears, oranges, peaches, nectarines, strawberries, melons, ...) or drink fruit juice (for example, orange juice, grapefruit juice, ...)?

0 = never or occasionally (less than once a month)
1 = about once a week
2 = about two or three times a week
3 = about four or five times a week
4 = about once a day
5 = more than once a day

4) How often do you eat green or yellow vegetables (for example, green salad, lettuce, broccoli, asparagus, cabbage, corn, spinach, carrots, ...)?

0 = never or occasionally (less than once a month)
1 = about once a week
2 = about two or three times a week
3 = about four or five times a week
4 = about once a day
5 = more than once a day

SUBJECT NUMBER_____

BACKGROUND INFORMATION

1. Date of birth?_____

2. Height?_____ Weight?_____

3. What is your marital status?

__Single

__Married How long?_____

__Separated How long?_____

__Divorced How long?_____

__Widowed How long?_____

4. What is your current family size?_____

5. Number of people living at your residence?_____

6. What is your highest educational level: ___Grammar School

___High School

___Some College

___College Degree

___Graduate Work

___Other (Specify)_____

7. What is your occupation?_____

8. What is your spouse's occupation?_____

9. What is your approximate annual income? ___Under 10,000/year

___$10,000 - $15,000/year

___$15,001 - $20,000/year

___$20,001 - $30,000/year

___$30,001 - $40,000/year

___$40,001 - $ 50,000/year

___over $50,000/year

The questions on this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought in a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

1. In the last month, how often have you been upset because of something that happened unexpectedly?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

2. In the last month, how often have you thought that you were unable to control the important things in your life?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

3. In the last month, how often have you felt nervous and "stressed?"

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

4. In the last month, how often have you dealt successfully with irritating life hassles?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

5. In the last month, how often have you felt that you were effectively coping with important changes that were occuring in your life?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

6. In the last month, how often have you felt confident about your ability to handle personal problems?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

7. In the last month, how often have you felt that things were going your way?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

8. In the last month, how often have you found that you could not cope with all the things that you had to do?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

9. In the last month, how often have you been able to control irritations in your life?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

10. In the last month, how often have you felt that you were on top of things?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

11. In the last month, how often have you been angered because of things that have happened that are outside your control?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

12. In the last month, how often have you found yourself thinking about things that you have to accomplish?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

13. In the last month, how often have you been able to control the way you spend your time?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

14 In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

0	1	2	3	4
never	*almost never*	*sometimes*	*fairly often*	*very often*

1. Please rate the degree to which you agree or disagree with the following statements. If you agree strongly, you might pick "1," if you agree, but not strongly, you might pick "2" or "3." If you disagree, you would pick "5," "6," or "7," depending on how strongly you disagree. If you don't really agree or disagree, you would pick "4."

	Agree strongly						Disagree Strongly
1. I often feel lonely, like I don't have anyone to reach out to.	1	2	3	4	5	6	7
2. When I am unhappy or under stress, there are people I can turn to for support.	1	2	3	4	5	6	7
3. I don't know anyone to confide in.	1	2	3	4	5	6	7
4. I used to have close friends to talk to about things, but I don't anymore.	1	2	3	4	5	6	7
5. When I am troubled, I keep things to myself.	1	2	3	4	5	6	7
6. I am not a member of any social groups (such as church groups, clubs, teams, etc.).	1	2	3	4	5	6	7
7. It is often not worth the effort to try to change the way things are.	1	2	3	4	5	6	7
8. I think that one can control what happens to him/her.	1	2	3	4	5	6	7
9. In (my home/the home) it is easy to predict what will happen.	1	2	3	4	5	6	7
10. In my life, in general, I think it is worthwhile to try to affect the way things are.	1	2	3	4	5	6	7
11. There is no point in trying to regulate contact with people in (this/my) home.	1	2	3	4	5	6	7

Subject #: _____ Date:__ __/__ __/__ __

MILLER BEHAVIORAL STYLE SCALE

1. Vividly imagine that you are **afraid** of the dentist and have to get some dental work done. Which of the following would you do? Check **all** of the statements that might apply to you.

___ I would ask the dentist exactly what he was going to do.

___ I would take a tranquilizer or have a drink before going.

___ I would try to think about pleasant memories.

___ I would want the dentist to tell me when I would feel pain.

___ I would try to sleep.

___ I would watch all the dentist's movements and listen for the sound of the drill.

___ I would watch the flow of water from my mouth to see if it contained blood.

___ I would do mental puzzles in my mind.

2. Vividly imagine that you are being held hostage by a group of armed terrorists in a public building. Which of the following would you do? Check **all** of the statements that might apply to you.

___ I would sit by myself and have as many daydreams and fantasies as I could.

___ I would stay alert and try to keep myself from falling asleep.

___ I would exchange life stories with the other hostages.

___ If there was a radio present, I would stay near it and listen to the bulletins about what the police were doing.

___ I would watch every movement of my captors and keep an eye on their weapons.

___ I would try to sleep as much as possible.

___ I would think about how nice it's going to be when I get home.

___ I would make sure I knew where every possible exit was.

3. Vividly imagine that, due to a large drop in sales, it is rumored that several people in your department at work will be laid off. Your supervisor has turned in an evaluation of your work for the past year. The decision about lay-offs has been made and will be announced in several days. Check **all** of the statements that might apply to you.

___ I would talk to my fellow workers to see if they knew anything about what the supervisor's evaluation of me said.

___ I would review the list of duties for my present job and try to figure out if I had fulfilled them all.

___ I would go to the movies to take my mind off things.

___ I would try to remember any arguments or disagreements I might have had with the supervisor that would have lowered his opinion of me.

___ I would push all thoughts of being laid off out of my mind.

___ I would tell my spouse that I'd rather not discuss my chances of being laid off.

___ I would try to think which employees in my department the supervisor might have thought had done the worst job.

___ I would continue doing my work as if nothing special was happening.

4. Vividly imagine that you are on an airplane, thirty minutes from your destination, when the plane unexpectedly goes into a deep dive and then suddenly levels off. After a short time, the pilot announces that nothing is wrong, although the rest of the ride may be rough. You, however, are not convinced that all is well. Check **all** of the statements that might apply to you.

___ I would carefully read the information provided about safety features in the plane and make sure I knew were the emergency exits were.

___ I would make small talk with the passenger beside me.

___ I would watch the end of the movie, even if I had seen it before.

___ I would call for the stewardess and ask her exactly what the problem was.

___ I would order a drink or tranquilizer from the stewardess.

___ I would listen carefully to the engines for unusual noises and would watch the crew to see if their behavior was out of the ordinary.

___ I would talk to the passenger beside me about what might be wrong.

___ I would settle down and read a book or magazine or write a letter.

Health Screen Survey (HSS)

Please indicate which, if any of the following illnesses or medical conditions you have had in the past 20 years. Please indicate the approximate years for each that you have had. Years ago? Duration of problem?

High blood pressure _____
Heart Attack _____
Heart Disease _____
Stroke _____
Circulation Problems _____
Migraine Headaches _____
Skin Cancer _____
Dermatitis (skin problems) _____
Leukemia _____
Anemia _____
Other Cancer (Specify) _____
Tuberculosis _____
Diabetes _____
Bronchitis _____
Ulcers (GI) _____
Hernia _____
Liver Trouble _____
Stomach Problems _____
Bowel Problems _____
Asthma _____
Emphysema _____
Epilepsy _____
Thyroid Problems _____
Back Problems _____
Arthritis _____
Urinary Tract Infection _____
Alcoholism _____
Eye Trouble _____
Allergies _____
Parkinson's Disease _____

For any of these conditions that are still present, please indicate how much it interferes with your daily life.

High blood pressure 1 2 3 4 5 6 7
no interference a great deal of interference

Heart Attack 1 2 3 4 5 6 7
no interference a great deal of interference

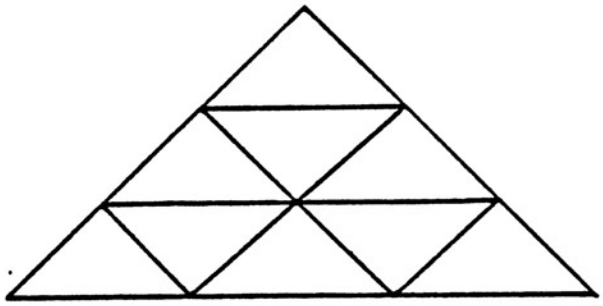
Heart Disease 1 2 3 4 5 6 7
no interference a great deal of interference

Stroke	1	2	3	4	5	6	7
	no interference						a great deal of interference
Circulation Problems	1	2	3	4	5	6	7
	no interference						a great deal of interference
Migraine Headaches	1	2	3	4	5	6	7
	no interference						a great deal of interference
Skin Cancer	1	2	3	4	5	6	7
	no interference						a great deal of interference
Dermatitis (skin problems)	1	2	3	4	5	6	7
	no interference						a great deal of interference
Leukemia	1	2	3	4	5	6	7
	no interference						a great deal of interference
Anemia	1	2	3	4	5	6	7
	no interference						a great deal of interference
Other Cancer	1	2	3	4	5	6	7
	no interference						a great deal of interference
Tuberculosis	1	2	3	4	5	6	7
	no interference						a great deal of interference
Anemia	1	2	3	4	5	6	7
	no interference						a great deal of interference
Diabetes	1	2	3	4	5	6	7
	no interference						a great deal of interference
Bronchitis	1	2	3	4	5	6	7
	no interference						a great deal of interference
Ulcers (GI)	1	2	3	4	5	6	7
	no interference						a great deal of interference

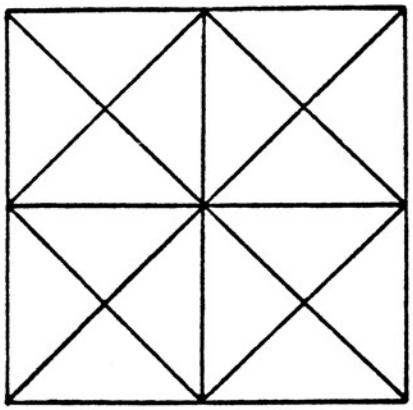
Hernia	1	2	3	4	5	6	7
	no interference						a great deal of interference
Liver Trouble	1	2	3	4	5	6	7
	no interference						a great deal of interference
Stomach Problems	1	2	3	4	5	6	7
	no interference						a great deal of interference
Bowel Problems	1	2	3	4	5	6	7
	no interference						a great deal of interference
Asthma	1	2	3	4	5	6	7
	no interference						a great deal of interference
Emphysema	1	2	3	4	5	6	7
	no interference						a great deal of interference
Epilepsy	1	2	3	4	5	6	7
	no interference						a great deal of interference
Thyroid Problems	1	2	3	4	5	6	7
	no interference						a great deal of interference
Back Problems	1	2	3	4	5	6	7
	no interference						a great deal of interference
Arthritis	1	2	3	4	5	6	7
	no interference						a great deal of interference
Urinary Tract Infection	1	2	3	4	5	6	7
	no interference						a great deal of interference
Alcoholism	1	2	3	4	5	6	7
	no interference						a great deal of interference
Eye Trouble	1	2	3	4	5	6	7
	no interference						a great deal of interference
Allergies	1	2	3	4	5	6	7
	no interference						a great deal of interference

Parkinson's Disease	1	2	3	4	5	6	7
	no interference						**a great deal of interference**

Feather Task. Figure 1



Feather Task: Figure 2



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